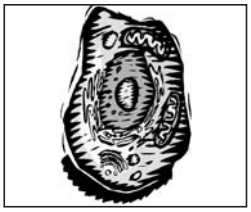

The Origin of Eukaryotic Cells

Michael Buratovich

The cells of modern organisms come in two main structural types: prokaryotic and eukaryotic. Prokaryotic cells, which are represented by the eubacteria and archaea, contain precious little internal compartmentalization and have transcriptionally coupled translation, whereas eukaryotic cells, which compose plants, fungi, algae, animals, and a widely diverse group of unicellular protists, are equipped with a large cadre of intracellular compartments that are functionally specialized for specific intracellular tasks.[1]

The origin of the more complicated eukaryotic cell type has been partially elucidated by the now widely-accepted endosymbiont theory, which posits that two of the major membrane-bound compartments of eukaryotic cells—mitochondria, the energy-making organelles, and chloroplasts, the organelles where photosynthesis occurs in plant cells—were formed from ancient bacteria that invaded the cytoplasm of an ancient proto-eukaryotic cell and eventually took up residence in that cell. Given the impressive molecular and genetic similarities between modern mitochondria and one specific group of bacteria, the α-proteobacteria,[2] and modern chloroplasts and cyanobacteria,[3] this hypothesis has won widespread acceptance among biologists and is a common staple of most high school and college biology textbooks.

While the endosymbiont theory is the best present answer to the question of eukaryotic cell origins, there is still widespread uncertainty regarding the identity of the original cell that hosted the initial endosymbiosis. The prevailing model asserts that the host cell initially invaded by those ancient bacteria that eventually became modern mitochondria had a nucleus, and, therefore, the genesis of mitochondria occurred after the formation of the nucleus and played no mechanistic role in nuclear formation.[4] However, problems abound with this scenario.[5]

In an attempt to resolve this mystery, William Martin and Eugene Koonin have devised a revolutionary and wonderfully novel hypothesis to explain the origin of the nucleus.[6] The following features of this hypothesis with the accompanying evidences that argue in its favor are outlined below. (Also, see Figure 1.)

1. *The original host of the initial endosymbiosis that led to mitochondria was a prokaryote related to the modern archaea and not a nucleated proto-eukaryote.*

Phylogenetic analyses of ribosomal RNAs strongly suggested that eukaryotes are a sister group of the archaea.[7] However, the utilization of different genes in another set of phylogenetic analyses suggested that eukaryotes are more closely related to the eubacteria.[8] An analysis with completely sequenced genomes has shown that eukaryotic genomes result, at least in part, from a fusion between archaeal and eubacterial genomes.[9]

Other studies not only corroborate the dual contribution of archaeal and eubacterial genes to eukaryotic genomes but also strongly suggest that the primitive cell that played host to the original α-proteobacterial invader did not have a nucleus. For example, those proteins specific to the nuclear envelope and components of the nuclear pore complexes, which allow the transport of large molecules to and from the nucleus, are cobbled together from protein domains specific to eubacteria and archaea, with various eukaryotic innovations.[10] Also proteomic

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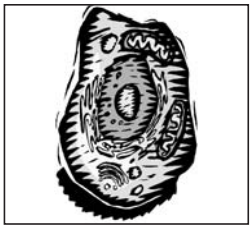
Michael Buratovich *holds B.S. and M.A. degrees in bacteriology and microbiology, respectively, from the University of California Davis and a Ph.D. in cell and developmental biology from the University of California Irvine. He also worked as a postdoctoral research fellow at Sussex University and at the University of Pennsylvania and presently is associate professor of biochemistry at Spring Arbor University. His research interests range from the tracheal system of the sow bug to iron metabolism in mitochondria. Buratovich is also a steady contributor to the contemporary debate over biological origins. He can be reached by email at: michaelb@arbor.edu*



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analyses of the proteins in the nucleolus, that dense portion of the nucleoplasm where ribosomal RNAs are transcribed and ribosome biogenesis occurs, have also demonstrated that these proteins are derived from eubacterial and archaeal ancestors.[11] These data are best explained if the nucleus and nucleolus arose in a cell that already contained a eubacterial endosymbiont as a source of eubacterial genes.

2. *The presence of transposable, self-splicing group II introns in the genomes of the invading bacterium posed problems for the host organism, since its genome was soon colonized and overrun by transposons whose excision was rather slow.*

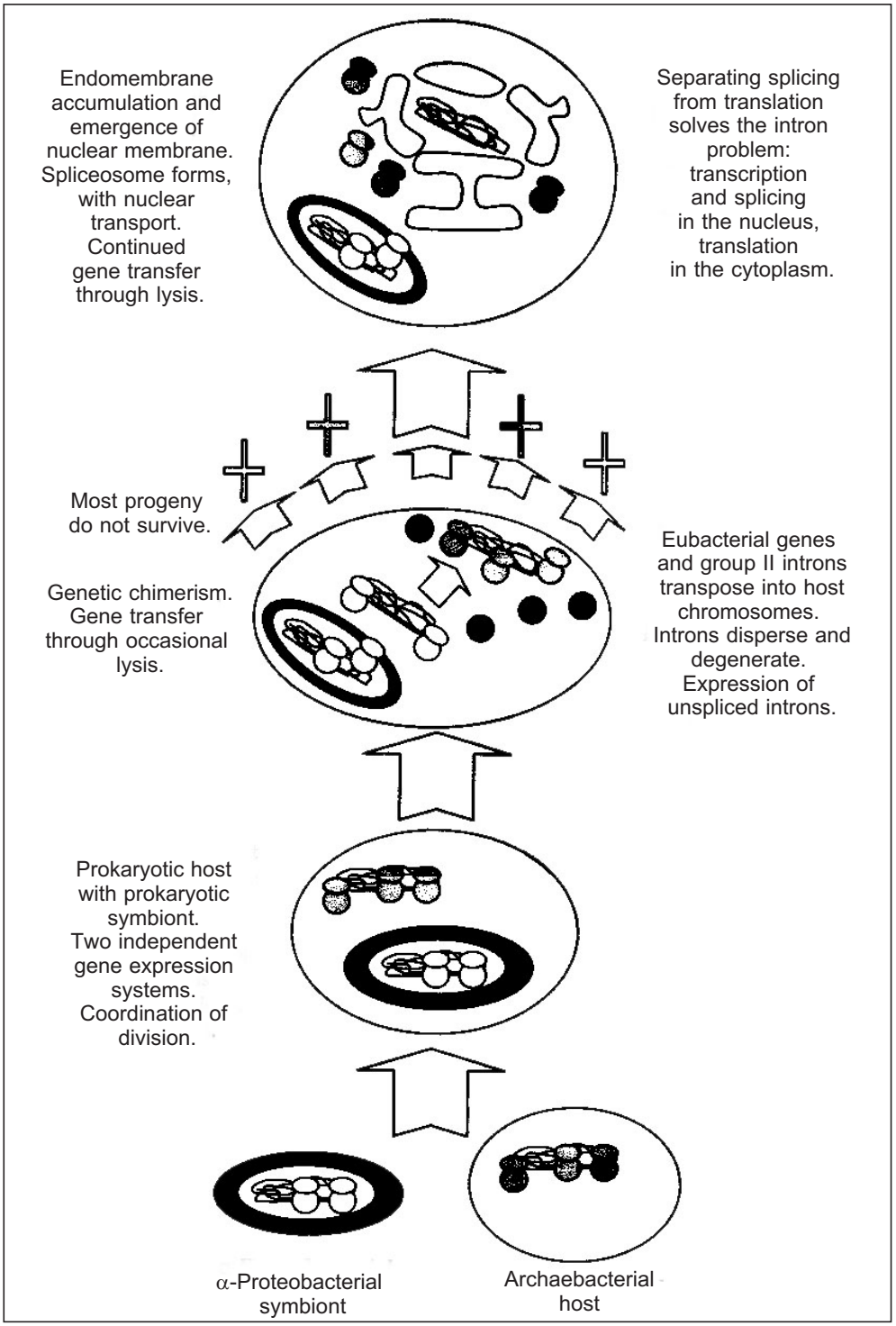


Figure 1

Modern eukaryotic genomes are loaded with intervening sequences called introns that interrupt coding sequences. Introns are initially transcribed when the initial messenger RNA (mRNA) is synthesized but are subsequently removed by a process called RNA splicing prior to nuclear transport of the mature mRNA to the cytoplasm for translation. RNA splicing is executed by a complex of proteins and small nuclear RNAs (snRNAs) called the spliceosome.[12]

Spliceosome-excised introns are widely viewed as having evolved from self-splicing group II introns. An impressive list of structural, biochemical, and functional similarities between group II introns and the processing of nuclear introns by the spliceosome supports this claim. First of all, the catalytic mechanisms employed by the two types of introns and their use of metal catalysts are strikingly similar.[13] Secondly, *in vitro* experiments have established that, like group II introns, the RNA component of the spliceosome forms its catalytic core.[14] Third, the metal-binding domain of II introns (domain V) can functionally substitute for the metal-binding portion of one of the RNA components (the U6atac snRNA stem-loop) of the spliceosome.[15] Finally, one of the RNA components of the spliceosome (snRNA U5) can functionally substitute for a particular portion of the group II intron (ID3 subdomain stem-loop).[16] These remarkable mechanistic resemblances and functional equivalences imply that spliceosome-dependent introns are the evolutionary descendants of group II introns.

Group II introns, however, are very common in eubacteria but extremely rare in the archaea.[17] Furthermore, group II introns are mobile genetic elements that can transpose from one location within a genome to another and require an intron-encoded reverse transcriptase/maturase protein for transposition and proper splicing.[18] If the host cell was a member of the archaea, its genome would have been bereft of introns. The invading α-proteobacterium, however, probably had several group II introns, just like their extant relatives. The transposition of these groups II introns into the genome of the host would have been inevitable, but would have also created problems for the host cell.

3. *The colonization of the host chromosomes with transposable type II introns led to a crisis in the life of these cells, since the excision of the intron was slow, but translation of the mRNAs made from these intron-infested genes was relatively fast, thus leading to the formation of junk protein.*

Messenger RNA splicing is a relatively slow process; modern splicing occurs at a rate of 0.005–0.1 introns removed per second.[19] However, translation is a relatively fast process, operating at a rate of one amino acid per second in modern eukaryotes.[20] Mutational inactivation of the intron-encoded maturase would have further slowed the process of splicing, but not stopped it completely, since the maturase can act in *trans*, but does so less efficiently.[21] Under these conditions, this early "proto-eukaryote" would have certainly made some nonfunctional protein.

The spliceosome components seem to have evolved from group II intron mRNAs and the Sm protein domain, which is involved in RNA-processing reactions in archaea.[22] The recruitment of Sm domain proteins to replace the function of the group II intron-encoded maturase provided the impetus for the formation of the spliceosome. The modern spliceosome contains some twenty paralogous Sm-domain-containing proteins, and this core complex is common to all eukaryotes and, therefore, must have been present in the last common ancestor of all eukaryotes.[23]

4. *Natural selection therefore pressured cells to physically separate the slow process of intron excision from the fast process of mRNA translation in order to preserve the integrity of gene expression.*[24]

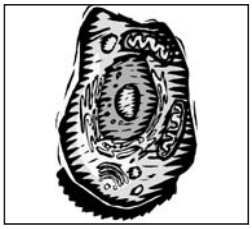
This early cell was under tremendous selective pressure to isolate the genome from the translational apparatus to prevent the constant synthesis of junk protein.

The nuclear envelope is contiguous with another internal cell membrane system: the endoplasmic reticulum. The cell uses the endoplasmic reticulum to initiate the syntheses of membrane-specific proteins, secreted proteins, membrane phospholipids and steroids. Gene duplication patterns suggest that the endoplasmic reticulum arose before the nucleus.[25] This means that the nuclear membrane might have resulted from the membranes of the already-existing endoplasmic reticulum aggregating around the region that contains the genome (nucleoplasm).[26] Once surrounded by these membranes, this barrier would have effectively isolated the genome from the translational machinery.

The formation of the nucleus in order to solve the problem of junk protein synthesis also potentially explains the origin of the nonsense-mediated decay (NMD) system in eukaryotes. The NMD system degrades incorrectly processed mRNAs and assures that only correctly processed mRNAs are translated into protein.[27] The formation of NMD as a direct consequence of interrupted genes makes sense and an examination of the NMD machinery shows components constructed from archaeal translation systems and eubacterial post-segregation killing systems.[28]

The Martin-Koonin hypothesis (MKH) of eukaryotic cell origins satisfyingly synthesizes a wide range of conflicting data. However, there are difficulties with this hypothesis. First of all, the MKH is contradicted by the observation that translation occurs in the nucleus,[29] but this is not a fatal objection since this result has been called into question.[30]

More importantly, the period of time before the formation of the nucleus and after the invasion of the genome by



The self-directing capacity of evolution is certainly compatible with a Creator-God who made heaven and earth and continues to sustain them. … [M]aterial hypotheses … cannot only provide fodder for further scientific inquiry, they can also help us tease out how God created the wonderfully complex and beautiful cells that compose all the plant and animal life …

group II introns represents an almost intractably deleterious hurdle for the proto-eukaryotic cell to clear. Clearly if the nucleus formed after the invasion of the "proto-mitochondrion," not only would this cell and its descendants not have fared well for some time, but it potentially would have been driven to extinction by stiff competition from its faster-growing and more efficiently operating prokaryotic neighbors. Many of its progeny would have died as the cell searched for strategies to mitigate its junk-protein problem. For the MKH to be correct, the formation of the nucleus must have occurred rather quickly after the invasion by the cell that gave rise to the mitochondrion.

Also, the MKH depends upon the existence of a proto-endoplasmic reticulum to aid in the formation of the nuclear membrane. This potentially explains why the outer leaf of the nuclear membrane is contiguous with the endoplasmic reticulum, but also postulates the existence of a complex organelle that is not found in extant archaea.

Fourth, members of an extant group of eubacteria called the planctomycetes possess bonified nuclei, which shows that endosymbiosis is not necessary for the formation of a nucleus.[31]

Finally, an examination of "eukaryotic signature proteins," in the organelles of eukaryotic cells has shown that the proteins of eukaryotic cells are not simply admixtures of sequences from archaea and eubacteria, but are, in many cases, unique in their own right. This makes the notion that the genomes of eukaryotes are simple combinations of eubacterial and archaeal genes unlikely.[32] Despite these drawbacks, Martin and Koonin's hypothesis is a fresh, new and thought-provoking piece of theorizing that should spur new experimental examinations into eukaryotic cellular origins.

Not everyone is enthusiastic about the endosymbiont theory. Young-earth creationist Don Batten, for example, writes that we should expect that

> there would be many similarities in many of the genes for photosynthesis or respiration between prokaryotes and eukaryotes—they have to achieve the same chemistry … Furthermore they have the same Designer.[33]

Batten concludes his critique of the endosymbiont theory by insisting that

> it is the atheistic bias of modern practitioners of science that prevents them from seeing the abundant evidence, right under their noses, for the unseen Creator of life.[34]

He implicitly argues that individuals who accept the mainstream interpretation of the large body of evidence that argues in favor of the endosymbiont theory do so because of a predisposed atheistic bias.

This convenient dismissal of the endosymbiont theory ignores the deep molecular similarities between modern mitochondria and chloroplasts and members of specific groups of extant eubacteria; similarities that have little to do with their chemistry. Secondly, Batten patently ignores modern examples of microorganisms that are presently in the process of becoming organelles, which constitute intermediates in organelle formation.[35] These data are best explained by postulating an ancestral relationship between these contemporary organelles and ancient bacteria. While we might wholeheartedly agree with Batten that prokaryotes, mitochondria, and chloroplasts have the same Designer, such an assertion does not tell us how the Designer went about fashioning them.

Even more troubling is the assumption that by searching for nature-bound causes to the origin of various cell types, we are somehow putting God out of a job. On the contrary, God's creative work does not end with the initial creation. Psalm 104:30 declares: "When you send your Spirit, they are created, and you renew the face of the earth" (NIV). Thus God not only sustains the universe but is active in the process of its continuous creation.[36] John Polkinghorne suggests that God influences creation through the input of active information, which gives form, place and time to matter.[37] Robert John Russell goes one step further and proposes that God inserts this information at the level of quantum indeterminacy so that quantum particles act in one manner and not another.[38] Niels Gregerson has argued that evolution is a self-organizing process that God directs from within.[39]

Thus the self-directing capacity of evolution is certainly compatible with a Creator-

God who made heaven and earth and continues to sustain them. Furthermore material hypotheses like the MKH cannot only provide fodder for further scientific inquiry, they can also help us tease out how God created the wonderfully complex and beautiful cells that compose all the plant and animal life we see on this planet. ▣

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