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Review

Predation and eukaryote cell origins: A coevolutionary perspective

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ABSTRACT

Cells are of only two kinds: bacteria, with DNA segregated by surface membrane motors, dating back ~3.5 Gy; and eukaryotes, which evolved from bacteria, possibly as recently as 800–850 My ago. The last common ancestor of eukaryotes was a sexual phagotrophic protozoan with mitochondria, one or two centrioles and cilia. Conversion of bacteria (= prokaryotes) into a eukaryote involved ~60 major innovations. Numerous contradictory ideas about eukaryogenesis fail to explain fundamental features of eukaryotic cell biology or conflict with phylogeny. Data are best explained by the intracellular coevolutionary theory, with three basic tenets: (1) the eukaryotic cytoskeleton and endomembrane system originated through cooperatively enabling the evolution of phagotrophy; (2) phagocytosis internalised DNA-membrane attachments, unavoidably disrupting bacterial division; recovery entailed the evolution of the nucleus and mitotic cycle; (3) the symbiogenetic origin of mitochondria immediately followed the perfection of phagotrophy and intracellular digestion, contributing greater energy efficiency and group II introns as precursors of spliceosomal introns. Eukaryotes plus their archaebacterial sisters form the clade neomura, which evolved from a radically modified derivative of an actinobacterial posibacterium that had replaced the ancestral eubacterial murein peptidoglycan by N-linked glycoproteins, radically modified its DNA-handling enzymes, and evolved cotranslational protein secretion, but not the isoprenoid-ether lipids of archaebacteria. I focus on this phylogenetic background and on explaining how in response to novel phagotrophic selective pressures and ensuing genome internalisation this prekaryote evolved efficient digestion of prey proteins by retrotranslocation and 26S proteasomes, then internal digestion by phagocytosis, lysosomes, and peroxisomes, and eukaryotic vesicle trafficking and intracellular compartmentation.

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Abbreviations: LGT, lateral gene transfer; ERAD, *ER*-*a*ssociated *d*egradation of proteins; SR, signal-recognition-particle receptor; NE, nuclear envelope.

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The origin of eukaryotes (eukaryogenesis) was the largest reorganization of cell structure ever. To explain it we must answer six questions: (1) When did they evolve? (2) What was the nature of the last common ancestor of all eukaryotes (the cenancestral eukaryote)? (3) What were its ancestors? (4) What were the physical mechanisms of the changes? (5) What were the major steps involved? (6) What triggered such exceptionally disruptive but seminal changes? This cannot be done in detail here, as ∼5000 novel genes originated during the origin of eukaryotes, the most dramatic genetic explosion in history (Makarova et al., 2005; Yang et al., 2005; Cavalier-Smith, 2007a), and I have only ∼9000 words.

Fortunately, not all genes are equally fundamental, and understanding eukaryogenesis is not nearly as difficult as often made out. Elements of a sound explanation already exist through advances in ultrastructure, molecular and cell biology, genetics, phylogeny, and theoretical analyses over 40 years. Persisting problems are that bacteria are so small that their cell biology lags greatly behind that of eukaryotes and we do not know the functions or 3D structure of many important structural proteins; lipid membrane dynamics that endow cells with form and integrity are also insufficiently understood.

Eukaryogenesis poses the problem how and why, just once in the history of life, cells radically spatially reorganized their membrane, skeleton, and chromosomal relationships. The origin of an endoskeleton, membrane budding and fusion, and a novel mode of feeding were fundamental. Table 1 summarises 60 innovations that eukaryogenesis theories must explain. Rather than trying to explain each in detail I focus on five things: (1) setting the phylogenetic scene; (2) showing how the different changes were logically interconnected; (3) emphasizing that twin themes of disruption and continuity underlie a coherent explanation; (4) explaining in more detail than hitherto the earliest steps in endomembrane origins associated with the evolution of phagotrophy; (5) arguing that these were probably preceded by a simpler predatory stage with internal digestion mediated by retrotranslocation and improved proteasomes.

I use the classical term bacteria as a simpler synonym for prokaryote (Cavalier-Smith, 2007b), i.e. embracing both classical bacteria and cyanobacteria, which prior to invention of that name (Stanier, 1974) were called blue-green algae or Cyanophyta, and also archaebacteria, renamed archae (Woese et al., 1990). See also discussion in Cavalier-Smith, 1991a,b.

1. Dating eukaryote origins

The oldest indubitably eukaryotic fossils are vase-shaped, e.g. *Melanocyrillium*; their oldest secure date for numerous well-preserved specimens is 760 My ago (Porter and Knoll, 2000). They are almost certainly shells of testate amoebae constructed by pseudopodial activity that never occurs in bacteria. Claims that they are arcellinid amoebae (phylum Amoebozoa) and euglyphid amoebae (phylum Cercozoa) (Porter et al., 2003) are highly questionable. None are confidently morphologically euglyphids (those suggested to be could be another group with agglutinated shells); no marine arcellinids are known, yet these fossils are all marine. Moreover, they apparently became extinct before the Phanerozoic. Most likely they were an extinct group of testate amoebae that flourished before Foraminifera evolved (Cavalier-Smith, in press). Possibly, Cryogenian glaciations that largely or entirely covered the globe in several kilometres of ice periodically from ∼710 to 635 My ago extinguished them (snowball earth). The only fossils confidently assignable to a modern eukaryotic phylum all postdate the melting of snowball earth (Cavalier-Smith, 2006a). The first are red algae (Rhodophyta) about 600 My old. Earliest animals date from ∼550 My, but most phyla only appeared after 530 My during the Cambrian explosion (most animals, some protozoa, e.g. Foraminifera, Radiozoa, green algae) or substantially later (land plants). A few poorly dated *Melanocyrillium*-like fossils date from ∼800 My, but relatively numerous deposits dated 850 My are devoid of them or anything definitely eukaryotic. Thus the most conservative estimate of the age of eukaryotes is 850–800 My ago (Cavalier-Smith, 2002a,c). That they are as old as bacteria (Kurland et al., 2006) is disproved by the fossil evidence.

In marked contrast there is unequivocal evidence for oxygenic photosynthetic prokaryotes as early as 2.45 Gy ago; most palaeontologists think cyanobacteria arose earlier, 2.9–2.7 Gy ago. No convincing evidence shows life before 3.5 Gy, currently the best estimate of when life began. Thus bacteria are probably four times as old as eukaryotes, making it certain that eukaryotes evolved from bacteria, not the reverse (Cavalier-Smith, 2006a). Even were optimistic identifications of a few meagre fossils ∼1.5 Gy ago as eukaryotic (Javaux et al., 2001) justified (I think not), bacteria would be 2.3× as old as eukaryotes.

No molecular biological 'clock' ticks constantly throughout geological time. Proteins evolve at rates differing over many orders of magnitude. As new proteins all evolve from old ones by gene duplication, rates must change dramatically over time. They change systematically among different branches of the tree and also episodically. When new paralogues arise, evolution is initially very fast as novel functions are acquired, e.g. during eukaryogenesis the ancestral RNA polymerase evolved into RNA polymerases I, II and III divergently adapted for transcribing rRNA, mRNA and tRNA; as distinct functions became perfected initial fast evolution gave way to much slower more trivial divergence. The bigger the functional shift the more dramatic the transient initial acceleration, a >10,000 fold increase in rate being likely for molecules like tubulins and actins that arose from bacterial FtsZ and MreB by multiple duplications (Amos et al., 2004; Erickson, 2007). Similar transient increases occur in rRNA. Many evolutionary misinterpretations stem from treating sequence divergence as clock-like (Cavalier-Smith, 2002c). Averaging rates of change in local parts of the tree allows useful interpolation between known fossil dates, but extrapolating backwards beyond fossil calibration points is extremely unreliable, providing no useful information beyond what fossils directly say, yet giving false confidence in inferences (Graur and Martin, 2004; Roger and Hug, 2006). It is scientifically unsound to use a 'clock' of tick-rate unknown by a factor of 10,000.

2. Eukaryote phylogeny and the properties of the earliest eukaryotes

To infer the nature of the first eukaryote rigorously we must locate the root of the eukaryotic tree confidently. This has been difficult, with many false trails. For a century, the first eukaryotes were variously postulated to be algae, fungi or protozoa; if protozoa, anaerobic or aerobic amoebae, flagellates or amoeboflagellates have each been considered primitive. It is well established that mitochondria evolved by symbiogenetic cell enslavement (Cavalier-Smith, 2006b, 2007a) from α-proteobacteria, which have the most mitochondrion-like respiratory chain (John and Whatley, 1975) and include purple non-sulphur photosynthetic bacteria. Sequence phylogeny (Keeling et al., 2005; Rodríguez-Ezpeleta et al., 2007) has revealed major clades of the eukaryote tree that are congruent with much ultrastructural data and helps position its root (Fig. 1). All known groups of anaerobic eukaryotes had ancestors that were at least facultatively aerobic with oxidative phosphorylation in mitochondria; in various protozoa and fungi mitochondria were subsequently polyphyletically modified as hydrogenosomes