Evolutionary cell biology: functional insight from "endless forms most beautiful"

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ABSTRACT **In animal and fungal model organisms, the complexities of cell biology have been analyzed in exquisite detail and much is known about how these organisms function at the cellular level. However, the model organisms cell biologists generally use include only a tiny fraction of the true diversity of eukaryotic cellular forms. The divergent cellular processes observed in these more distant lineages are still largely unknown in the general scientific community. Despite the relative obscurity of these organisms, comparative studies of them across eukaryotic diversity have had profound implications for our understanding of fundamental cell biology in all species and have revealed the evolution and origins of previously observed cellular processes. In this *Perspective*, we will discuss the complexity of cell biology found across the eukaryotic tree, and three specific examples of where studies of divergent cell biology have altered our understanding of key functional aspects of mitochondria, plastids, and membrane trafficking.**

Monitoring Editor
David G. Drubin
University of California, Berkeley

Received: May 18, 2015
Revised: Aug 21, 2015
Accepted: Aug 22, 2015

The field of cell biology has made tremendous strides in understanding eukaryotic cells, especially animals and yeast. Concurrently, evolutionary biology has opened up a window to the origins of our species and the genes that define us. Though these fields have intersected conceptually for decades, a recent movement is explicitly uniting these two fields into the discipline of evolutionary cell biology with great success (Brodsky *et al.*, 2012; Lynch *et al.*, 2014) and, we argue here, potentially an even greater future. One drive behind this movement is to harness the comparative approach of evolutionary biology and apply it to questions of cellular origins and cellular function. This approach has yielded beautiful insight into animal cellular function from mitotic spindle dynamics (Helmke and Heald, 2014) to glycosylation machinery (Varki, 2006). However, expanding the scope of investigation to organisms beyond fungi and animals to span eukaryotic diversity has allowed for discoveries that force us to adjust some fundamental ideas of how eukaryotic organelles work, and why.

DOI:10.1091/mbc.E14-10-1433

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Abbreviations used: AP, adaptor protein; CIA, cytosolic iron–sulfur assembly; LECA, last common eukaryotic; ancestor; MROs, mitochondria-related organelles; NIF, nitrogen fixation; SUF, sulfur utilization factor.

EUKARYOTIC DIVERSITY: FROM ANIMACULES TO AMITOCHONDRIATES

From van Leeuwenhoek's description of his "animacules" soon after the development of the microscope, cell biology has always been linked with single-celled organisms. Nonetheless, studies of cell biology and physiology remain restricted to relatively few model organisms, such as flies, worms, yeasts, and human cells, often closely related to humans and manipulated under restrictive circumstances (Del Campo *et al.*, 2014). This means that pathways and mechanisms assumed to be essential from their presence in conventional model organisms may actually be divergent or lineage specific, and this can lead to unjustified extrapolation of cell biological principles beyond their actual range. Conversely, because our knowledge is so heavily based on taxonomically restricted model systems, we may be missing key cell biological components, pathways, or phenomena in cells beyond humans and yeast, or overlooking potentially important aspects of our own cellular biology.

Reaping the benefit of the vast amounts of genomic data now available from diverse organisms, evolutionary biologists have performed large-scale molecular evolutionary analyses. Together with morphological information from light and electron microscopy, this molecular information has been used to establish the eukaryotic tree outlined in Figure 1 and to formalize a coherent framework for eukaryotic relationships (Adl *et al.*, 2012).

Most model cell biological systems (flies, worms, yeast and human cells) are grouped within the supergroup Opisthokonta (Figure 1). However, this only scratches the surface of eukaryotic

diversity. While the taxonomy may be daunting, the organisms classified outside Opisthokonta have tremendous medical importance (including parasites of global health relevance), agricultural relevance (both plants and their pathogens), and ecological implications (key players in all known food webs). Understanding eukaryotic diversity is to understand critical aspects of the world in which we live. The opisthokonts are related to two lineages of single-celled flagellates, apusozoa and breviates (Brown *et al.*, 2013), and the amoebozoans, a group containing ecologically relevant soil microbes and pathogenic organisms (e.g., *Entamoeba histolytica*, the causative agent of amebic dysentery, and *Dictyostelium*, an emerging cell biological model organism and an important constituent of forest ecosystems). Archaeplastids (Figure 1) encompass multicellular plants and green algae within the Viridiplantae, but also the red algae (rhodophytes), which include many cultivated and edible seaweed species (e.g., nori), and glaucophyte algae. Stramenopiles, alveolates, and rhizarians are grouped within the SAR supergroup, related to archaeplastids (Figure 1). The SAR supergroup contains many parasitic species, including the malaria-causing *Plasmodium falciparum*, as well as diatoms and dinoflagellates that play an absolutely vital role in nutrient cycling in aquatic ecosystems. The final two eukaryotic supergroups are less securely placed. The controversial CCTH supergroup is thought to be most closely related to the SAR and archaeplastid supergroups and tentatively contains algae such as the cryptophytes and haptophytes. The latter can grow in blooms large and dense enough to be visible from space. The CCTH supergroup may contain lesser-known marine organisms such as the centrohelids and telomerids, but our understanding of the relationships between these four lineages is in relative flux. The last supergroup,

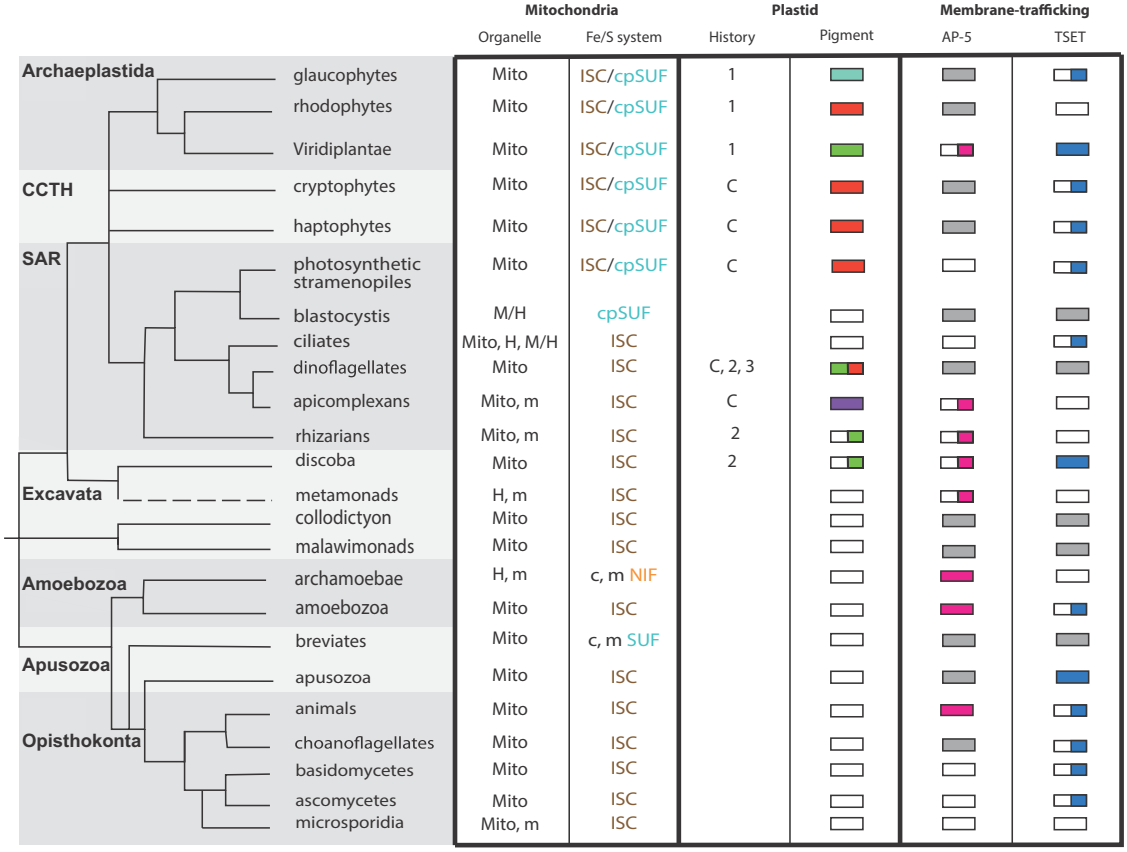

FIGURE 1: Diversity of aspects of cell biology across eukaryotes. Phylogenetic relationships of major eukaryotic lineages, with emphasis on lineages highlighted by cell biological examples. The rooting is shown within the supergroup Excavata, with Discobans on one side and Malawimonads and *Collodictyon* on the other. The relationships shown are based on information from Adl *et al.* (2012), Brown *et al.* (2013), and Derelle *et al.* (2015). The table illustrates the diversity of the cell processes discussed in this review. Column 1 (Mitochondria): type of mitochondria present in the lineage. Mito, conventional mitochondria; M/H, a mitochondria/hydrogenosome-like organelle; H, a hydrogenosome; m, a mitosome. Column 2 (Fe/S System): Fe/S production system present in the cell and its localization. ISC, a conventional iron/sulfur cluster pathway; cpSUF, a SUF system localized in the chloroplast; cSUF, a SUF system localized in the cytosol; c, m NIF, a NIF system localized to the chloroplast and mitosome; and c, m SUF, a SUF system localized to the cytosol and mitosome. Column 3 (History): number of endosymbiotic events involved in establishment of plastids in the lineage; chromalveolate plastids, where the exact phylogenetic derivation is currently unknown, have been indicated with a "C." Column 4 (Pigment): presence or absence of a plastid and, if present, evolutionary affinity of the plastid. Red denotes plastids of red algal origin; green denotes plastids of green algal origin; teal indicates plastids that are ancestral to the red and green lineages; purple indicates that this is a plastid of red algal origin, but is no longer photosynthetic. Multiple colors indicate the presence of multiple plastid types within the taxonomic group. Column 5 (AP-5): complete presence, partial presence, or absence of AP-5, respectively represented by fully colored, half-colored, or white. Gray indicates taxa not searched for AP-5. Column 6 (TSET): complete presence, partial presence, or absence of TSET, respectively represented by fully colored, half-colored, or white. Gray indicates taxa not searched for TSET.

Excavata, includes important parasites, such as the diarrheal agent *Giardia* and the agent of African sleeping sickness, *Trypanosoma brucei*.

FUNCTION AND DIVERSITY: HOW ONE INFORMS THE OTHER

The question of which eukaryotic lineage is the most ancient (i.e., where the root of the tree of eukaryotes is placed) has important implications for how one interprets cell biological data between organisms and across evolutionary time. Cell biological traits observed in the various eukaryotic supergroups are most logically interpreted with the starting state being at the root and change inferred from there. The latest and most robust molecular evolutionary analyses place Excavata straddling the root of eukaryotes (Figure 1), which would place an ancient divide between its members (Derelle *et al.*, 2015). This rooting implies that the last common eukaryotic ancestor (LECA) had a complex set of cytoskeletal arrangements and was likely biflagellated (Yubuki and Leander, 2013; Derelle *et al.*, 2015), as this is the cell biology we observe across eukaryotes, even in lineages that diverged extremely early in evolutionary history. Comparative molecular evolutionary studies also reconstruct a LECA that is anything but simple or primitive. Analyses of proteins associated with nuclear function, membrane trafficking, metabolism, and more have reconstructed a sophisticated complement of machinery present in the LECA (Koumandou *et al.*, 2013), estimated to have been in existence ~1.5 billion years ago (Eme *et al.*, 2014).

Delving into this complexity, particularly in organisms for which genomic information can be combined with molecular cell biological analyses, has provided surprising findings about the biology and function of modern cells. We highlight three examples below, showing the different ways in which an evolutionary cell biological approach can be fruitful. In the first two examples, organisms with divergent organelles were studied in order to better understand the evolution and diversity of organellar function. In the last case, purely exploratory studies of genomic and cell biological diversity revealed unforeseen cellular components and pathways.

MITOCHONDRIA: HIGHLY RETAINED, BUT WHY?

Best known as the powerhouse of the cell, due to its involvement in aerobic respiration and energy generation, mitochondria were among the first organelles to capture the attention and inspiration of evolutionary cell biologists. Evolutionary analysis was key to the startling discovery in the 1980s that these organelles derived from an endosymbiotic alpha-proteobacterium and the further revelation (Muller *et al.*, 2012, among others) that the diverse double membrane–bound organelles in disparately related anaerobic eukaryotes are, in fact, derived mitochondria. Hydrogen-producing organelles (i.e., "hydrogenosomes") are found in ciliates, members of the SAR supergroup, and in several members of the Excavata group, including *Trichomonas* (Figure 1). The even more reduced mitochondria, so-called mitosomes, are found in diverse groups, including the metamonad *Giardia*, the amoebozoan *Entamoeba*, the apicomplexan *Cryptosporidium*, and the opisthokont microsporidia (Figure 1). These mitochondria-related organelles (hereafter collectively called MROs) can be found in at least one taxon in almost all eukaryotic supergroups (Figure 1) and may harbor no more than 130 proteins (Jedelský *et al.*, 2011) out of 1200 that are usually found in canonical mitochondria. Contrary to the well-known role of mitochondria, some MROs are not involved in energy generation at all; some may "steal" ATP from the organism's cytosol in order to function (Tsaousis *et al.*, 2008). That all currently investigated eukaryotes appear to contain MROs raises questions about the "essential" function of the organelle; if not energy generation, then what?

Proteomic analyses of mitochondria and MROs (Sickmann *et al.*, 2003; Heazlewood *et al.*, 2004; Smith *et al.*, 2007; Jedelský *et al.*, 2011) have demonstrated that formation and export of iron–sulfur (Fe-S) clusters, essential for several enzymatic catalyses and regulation of gene expression, are the only universally conserved biosynthetic pathway localized within these organelles (Hjort *et al.*, 2010). Although iron and sulfur can be assembled in nature, the individual components are toxic for the cell itself. In typical eukaryotes, the mitochondrial iron–sulfur cluster (ISC) biosynthetic machinery is responsible for the assembly of Fe-S clusters in the mitochondria and supports the cytosolic iron–sulfur assembly (CIA) machinery (Figure 2Ai), for the assembly of the cytosolic and nuclear Fe-S clusters. It is now widely accepted that the ISC could be the raison d'etre of these organelles (Lill *et al.*, 2005).

In microbial eukaryotes, the story is more complicated. Despite the presence of ISC machinery and export in all mitochondria and most MROs, including remnant organelles (Goldberg *et al.*, 2008), new Fe-S cluster biosynthetic machineries have recently been described in microbial eukaryotes. *Blastocystis*, an anaerobic member of the SAR supergroup (Figure 1), encodes a fused version of the components of the sulfur utilization factor (SUF) system (Figure 2Aii; Tsaousis *et al.*, 2012). This system, which is also involved in Fe-S cluster formation but is evolutionarily unrelated to the ISC machinery, is typically found in bacteria, methanoarchaea, and plastid-bearing organisms. The SUF machinery localizes in the cytosol of *Blastocystis* and is induced under oxygen stress conditions (Tsaousis *et al.*, 2012), potentially affecting the CIA machinery protein composition and function (Tsaousis *et al.*, 2014). A similar acquired system was also found in the free-living breviate *Pygsuia biforma* (Figure 1), but here the SUF machinery is also mitochondrially localized (Stairs *et al.*, 2014; Figure 2Aiii) and the ISC machinery appears to be absent.

Finally, in the amoebozoans (Figure 1) *Entamoeba* and *Mastigamoeba*, the ISC system is also nonexistent; instead a nitrogen fixation (NIF)-related system from epsilon-proteobacteria is localized both to the MROs and the cytosol (Figure 2A, iv and v; Maralikova *et al.*, 2010; Nývltová *et al.*, 2013). This calls into question the purpose of the ISC and CIA pathways in the origin and existence of ancestral mitochondria. The reasons for modifications are undetermined, but alternations in environmental oxygen levels could have played a fundamental role in their acquisition, selection, and retention.

Although energy production is presently accepted as the driver for the origin of mitochondria (Lane and Martin, 2010, but see Gray, 2014, for an intriguing alternative), it appears to be Fe-S cluster assembly that is the organelle's conserved essential function (Lill *et al.*, 2005; Embley and Martin, 2006). Still, with 25–40% of proteins being of unknown function in all MROs studied to date (Sickmann *et al.*, 2003; Heazlewood *et al.*, 2004; Smith *et al.*, 2007; Jedelský *et al.*, 2011; Schneider *et al.*, 2011), investigating the "unknown functions" of mitochondria and MROs could yet provide us with some unexpected answers to understanding the origins and cellular role of this organelle.

PLASTID ACQUISITION: COMPLEX ENDOSYMBIOTIC HISTORY SHAPES PHYSIOLOGY

The other well-known endosymbiotic organelles are the chloroplasts or, more generically, plastids. Best known for their role as the site of photosynthesis in eukaryotes, they can carry out a number of

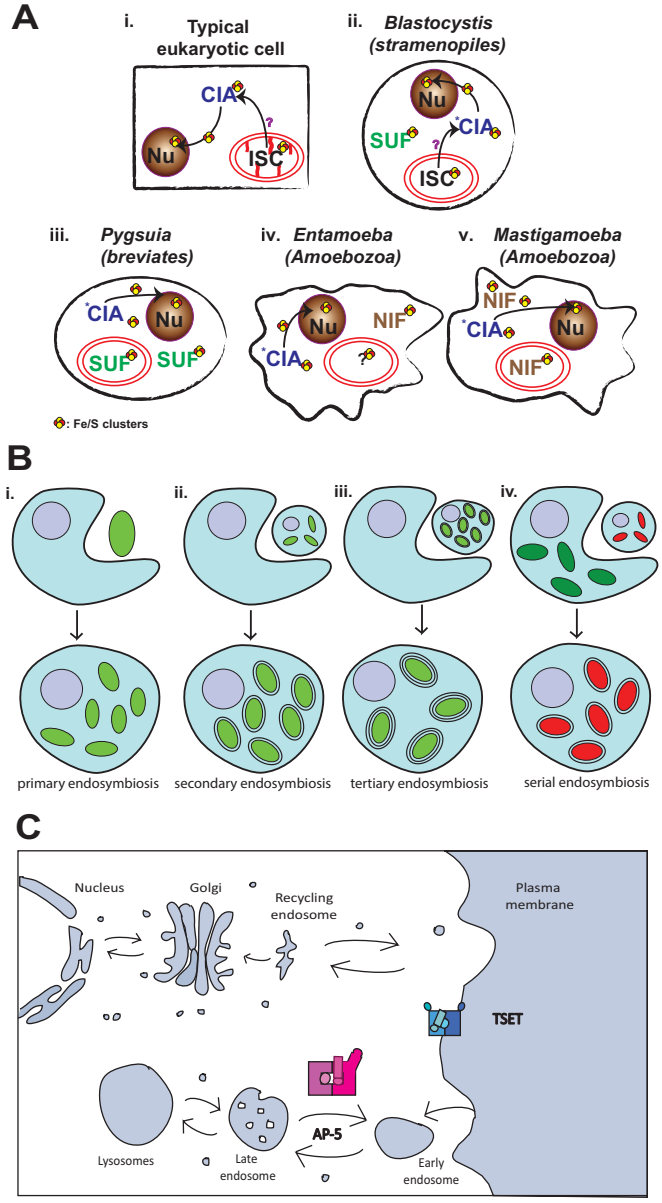

FIGURE 2: Illustrations of cell biological complexity. (A) Diagram demonstrating the alternative pathways of biosynthesis of Fe-S clusters in microbial eukaryotes. (i) A typical eukaryotic cell requires the ISC system to support the mitochondrial apo-(Fe-S)-proteins (proteins that require Fe-S clusters to be functionally active) and the CIA machinery for the cytosolic and nuclear apoproteins. (ii) *Blastocystis* requires a modified CIA machinery and the SUF machinery for the maturation of its cytosolic, nuclear, and oxygen-sensitive apoproteins. (iii) *Pygsuia* has the SUF machinery localized in its mitochondria instead of the typical ISC machinery for the support of the organellar apoproteins. (iv) *Entamoeba* has lost the traditional ISC machinery and has acquired NIF machinery in its cytosol for the support of their apoproteins. (v) *Mastigamoeba* has lost the traditional ISC machinery and has acquired two NIF machineries in its cytosol and its hydrogenosome for the support of their apoproteins. (B) Diagram demonstrating various methods of plastid acquisition found in various lineages. (i) Primary endosymbiosis, in which a cyanobacteria is engulfed by a heterotrophic eukaryote, resulting in establishment of chloroplasts. (ii) Secondary endosymbiosis, in which a photosynthetic eukaryote is engulfed by a heterotrophic eukaryote, resulting in establishment of chloroplasts. Other cell structures from the original eukaryote may also remain. (iii) Tertiary endosymbiosis, in which a photosynthetic organism containing a secondary plastid is itself engulfed by another eukaryote, to produce a plastid. (iv) Serial endosymbiosis, in which a photosynthetic eukaryote is engulfed by another photosynthetic eukaryote. This results in the establishment of a replacement chloroplast of a different phylogenetic derivation. (C) Diagram of a eukaryotic membrane-trafficking system. Major endomembrane organelles are labeled; trafficking pathways are denoted by curved arrows. Localization and structure of TSET and AP-5 indicated by blue and magenta structures, respectively. All adaptin complexes and TSET and COPII share a heterotetrameric quaternary structure of two large subunits and a medium and a small subunit as illustrated for AP-5 and TSET. The FCHO of animals is derived from the TSET medium subunit (drawn here as the blue exclamation point–shaped component). The shared quaternary structure and sequence conservation between subunits of the complex is evidence of their being derived from an ancient common ancestor. Recent analyses have begun to resolve their interrelationships and, by inference, the evolutionary order of emergence for the pathways in which they act. For more details see Hirst *et al.* (2014).

other functions, including synthesis of cofactors (Fe-S clusters), fatty acids, and heme (Dorrell and Howe, 2012). The evolutionary history of a given plastid provides context for its cell biology, and thus the function of a key organelle in a dazzling array of ecologically and agriculturally important eukaryotes. Plastids initially arose from the endosymbiosis (Figure 2Bi) of a cyanobacterium by the common, heterotrophic ancestor of the archaeplastids (green algae, red algae, and plants), but their presence is not limited to this supergroup (Walker *et al.*, 2011). Members of the green and red algae were subsequently taken up and converted to organelles through higher-order endosymbioses (Figure 2Bii) by at least seven other eukaryotic lineages distributed across multiple supergroups (Figure 1).

Endosymbiosis was initially considered rare, due to it being "mutationally onerous" (Cavalier-Smith, 1999), and early evolutionary models accordingly minimized plastid acquisition. The chromalveolate hypothesis (Cavalier-Smith, 1999) explained the distribution of plastids by parsimoniously suggesting that the plastids of several ecologically important algal groups (cryptophytes, haptophytes, stramenopiles, and dinoflagellates) originated through a single, secondary endosymbiosis of a red alga. The use of chlorophyll *c* as a light-harvesting pigment suggests their common origin, as do plastid gene phylogenies that consistently recover monophyletic relationships between these chloroplast lineages (Bachvaroff *et al.*, 2014). However, evidence has come to light in the last decade that the story may be more complex than it first appeared.

Multigene phylogenies of nuclear genes have conclusively shown that each of the putative chromalveolate lineages are more closely related to nonphotosynthetic eukaryotes than they are to each other. For example, the stramenopiles and dinoflagellates are very closely related to the rhizarians, a group composed almost entirely of nonphotosynthetic protists (Burki *et al.*, 2007). Multiple, independently conducted studies of nuclear and mitochondrial genomes have now rejected the monophyly of the putative "chromalveolate" lineages (Baurain *et al.*, 2010; Burki *et al.*, 2012; Stiller *et al.*, 2014). Some authors argue for a single ancestral acquisition in the common ancestor of chromalveolate and related lineages, with extensive loss (Cavalier-Smith, 1999).

Nonetheless, the monophyletic nature of chromalveolate plastids but disparate evolutionary origins of the corresponding nuclear lineages suggest a complex progression of endosymbiosis. Recent studies have found evidence for multiple endosymbiotic transfers

between different "chromalveolate" lineages. These studies suggest that an endosymbiosis of a red alga initially occurred within the cryptophyte algae and that this plastid was then acquired by other lineages (such as dinoflagellates, haptophytes, stramenopiles) through higher-order endosymbioses (tertiary or quaternary; see Figure 2Biii; Stiller *et al.*, 2014). There are even more complex endosymbiotic events known. Some dinoflagellates, for example, have lost their original plastids (presumably from red algae) and replaced them with ones derived from other photosynthetic algae (haptophytes, stramenopiles, and green algae) in a process termed "serial endosymbiosis" (Burki *et al.*, 2014; Figure 1). Regardless, the emerging story from these and other studies is that plastid endosymbiosis is a much more widespread and complex process than previously thought.

Resolving the evolutionary histories of plastids informs our mechanistic understanding of algal cell biology, since each time a plastid is acquired through endosymbiosis, both the biology of the plastid and host may change to accommodate one another. Proteins derived from the host are likely to be retargeted to the plastid, and genes from the plastid may in turn be adapted to support the biology of the host. Lineages that have undergone complex and serial endosymbiotic events may therefore be supported by a mosaic of different biochemical pathways from different evolutionary sources. For example, some dinoflagellates that have undergone serial endosymbiosis retain unusual gene expression pathways associated with their original, red algal plastids (RNA editing and 3′ tail addition) and now use these pathways in their replacement plastids (Dorrell and Howe, 2012). While these diverse algal lineages may be unfamiliar to many cell biologists, they are well-known to oceanographers and public health officials, accounting for half of primary carbon fixation worldwide and, in some cases, producing harmful algal blooms (Place *et al.*, 2012). As climate change modifies our oceans and skies, understanding the cell biology of these chimeric organisms forged through endosymbiosis will be essential for maintaining a healthy global environment.

UNEXPECTED MEMBRANE-TRAFFICKING MACHINERY: SOMETHING OLD, SOMETHING NEW

Although understanding endosymbiosis has been a key success of evolutionary cell biology in the past 40+ years, some organelles must have been derived from building blocks in the proto-eukaryotes themselves (Dacks and Field, 2007). The best candidates are organelles of the membrane-trafficking system. Consisting of membrane-bound components that include the endoplasmic reticulum, Golgi complex, lysosomes, endosomes, and the plasma membrane, the membrane-trafficking system is responsible for substance intake, transport within cells, and secretion from them. The system is critical for normal cellular function, and its malfunction in humans can manifest as diseases such as cancer and cardiac disease (Aridor and Hannan, 2000, 2002). Evolutionary analysis of the membrane-trafficking system has revealed the proteins of membrane trafficking (e.g., SNAREs, Rabs, coatomers, and adaptor proteins [APs]) to be conserved across eukaryotes (Koumandou *et al.*, 2013). This suggested the presence of sophisticated machinery in LECA, prompting a proposed mechanism for how organelles might evolve, if not by endosymbiosis (Dacks and Field, 2007). This approach to exploring diversity for the sake of evolutionary understanding has also yielded some surprises about membrane trafficking in modern cells.

Four heterotetrameric AP complexes have been known since 2001 to recruit specific cargoes to their corresponding, newly forming, vesicles for transport in the post-Golgi and endocytic system (Boehm and Bonifacino, 2001). However, a fifth AP (AP-5) was recently discovered. Together with the ancient nature of the other four, this indicates that the LECA contained at least five AP complexes (Hirst *et al.*, 2011). The twist is that the human genes encoding the subunits of AP-5 (Figure 2C) were known earlier but went unstudied until AP-5 homologues were detected in *Naegleria*, a discoban (Figure 1) of distant relation to humans that was of interest as a key evolutionary sampling point. This hinted at widespread occurrence and presumptive cellular importance, prompting functional investigation. Characterization in HeLa cells showed AP-5 localized to late endosomes and lysosomes (Figure 2C) with knockdown causing defects in endosomal trafficking (Hirst *et al.*, 2011). Abnormalities in AP-5 are consequently associated with human disease, such as hereditary spastic paraplegia (Hirst *et al.*, 2011, 2013). Further taxonomic investigation also detected AP-5 components beyond humans and *Naegleria*, in diverse eukaryotes (Figure 1) including *Arabidopsis* (Viridiplantae), *Entamoeba* (amoebozoan), and *Toxoplasma* (apicomplexan), suggesting that AP-5 is a central component of membrane trafficking in eukaryotic cells.

Following the discovery of AP-5 was the report of yet another relative of the APs, the heterohexameric TSET (Figure 2C). Analyses of TSET function in *Arabidopsis* and *Dictyostelium* showed TSET to be located at the plasma membrane, facilitating cargo transport (Gadeyne *et al.*, 2014; Hirst *et al.*, 2014). Similar to AP-5, TSET was detected across eukaryotic diversity and is thus ancient; by contrast, TSET is not as well retained as AP-5 in animals and fungi (Figure 1). Nevertheless, study of TSET revealed the origins of the human FCHO protein (Gadeyne *et al.*, 2014; Hirst *et al.*, 2014), which is important in endocytosis regulation. The monomeric FCHO appears to be the remnant of the once full TSET complex; essentially, FCHO is the vestigial C-terminus domain of the TCUP subunit, fused with an associated F-BAR domain that, in animal cells, had earlier been discovered to be involved in clathrin-mediated endocytosis at the plasma membrane (McMahon and Boucrot, 2011).

The search for distant homologues of known membrane-trafficking machinery that are found across the span of eukaryotic diversity did more than identify ancient cellular components. The broad evolutionary distribution of AP-5 and TSET components implied some conserved essential function and brought candidate genes to the fore, with the existence of these having since proven to have powerful implications. Other such genes exist and await functional characterization, hopefully with benefits for agriculture, ecology, or human health (Hirst *et al.*, 2014).

CONCLUSIONS

Evolutionary cell biology has provided unique insights into the core function of mitochondria, how history explains physiology of plastids, and the identity of novel membrane-trafficking complexes and pathways relevant to human health. Key to these findings has been the complementary use of genomic and informatic analyses with molecular cell biological and microscopic data. The emergence of model organisms from outside the animals and fungi has been invaluable in this regard. *Dictyostelium* (http://dictybase.org) and *Arabidopsis* (www.arabidopsis.org) are particularly well-developed systems; although not mentioned explicitly here, work in the apicomplexan *Toxoplasma gondii* (Kim and Weiss, 2004) and the excavate *Trypanosoma brucei* (Barry *et al.*, 2007) has greatly contributed to comparative cell biological understanding. The development of further genetic databases and tools for manipulating these organisms and others across the diversity of eukaryotes will provide experimental data to contextualize fundamental cellular traits and to

find new features lost or ignored in our more traditional model systems of animals and fungi. The discoveries of new organellar evolution and function gives us a taste of what may be left to uncover by embracing and exploring eukaryotic genomic and cellular diversity.

ACKNOWLEDGMENTS

We thank H. Goodson, T. Simmen, and J. Hirst for critical reading of the manuscript. A.T. is supported by a Biotechonology and Biological Sciences Reserach Council (BBSRC) Research grant: BB/M009971/1. R.G.D. is supported by a postdoctoral research fellowship from the Mairie de Paris. E.R. is supported by a Graduate Recruitment Scholarship from the University of Alberta Faculty of Medicine and Dentistry and funds to J.B.D. from Alberta Innovates Technology Futures. K.Z. is supported by a summer studentship from Alberta Innovates Health Solutions, and J.B.D. is the Canada Research Chair in Evolutionary Cell Biology. The quotation in the title of this *Perspective* is from Charles Darwin (*The Origin of Species*, 1859).

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