Mitochondria, complexity, and evolutionary deficit spending

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Lynch and Marinov (1) challenge our findings (2) that mitochondria are essential to the prokaryote–eukaryote transition. Their paper states: "Lane and Martin introduced the cost of a gene as an argument for the impossibility of high levels of cellular/developmental complexity without a power-generating mitochondrion." Scrutinizing bioenergetic costs, they conclude that "an energetic boost associated with the emergence of the mitochondrion was not a precondition for eukaryotic genome expansion" (1).

In fact, our paper (2) was not about the bioenergetic costs of a gene at all. We considered energy availability per gene: supply, not demand. Lynch and Marinov (1) fail to consider supply. Their calculations are interesting, but their conclusions about mitochondria and eukaryote complexity are untrue.

In terms of supply, bacteria are not ATP-deficient. However, if bacteria are scaled up to eukaryotic proportions, their energy availability per gene falls dramatically, because ATP synthesis depends on the surface area of bioenergetic membranes, whereas the cost of protein synthesis depends on cell volume (2). Even if the costs of protein synthesis fall slightly with volume, as argued (1), the ATP supply capacity of a eukaryote-sized bacterium to meet those costs falls by orders of magnitude, which severely restricts bacterial genome size and gene expression (2), explaining the lack of overlap between bacteria and eukaryotes in cell volume and genome size. In Lynch and Marinov's calculations (1), ATP synthesis is, inexplicably, unconstrained.

Bacteria with invaginated membranes have more surface area for generating ATP. Why don't they become "eukaryotic"? The difference relates to mitochondrial genes, which are indispensable for controlling respiration (3). As in 200,000-ploid giant bacteria (2), large cyanobacteria have hundreds of complete genome copies (4), positioned right next to bioenergetic membranes. The costs of extreme polyploidy, ignored by Lynch and Marinov (1), offset the advantage of increased surface area.

Consequently, giant bacteria are metabolically active only at their ATP-synthesizing cell surface (2). In eukaryotes, mitochondrial genome reduction and specialization allow ATP supply to scale freely with increased cell volume. Large cells with one nuclear genome, not thousands of cytosolic ones, could increase gene expression throughout their cytosol, supported energetically by mitochondria. Lynch and Marinov neglect the fundamental difference between prokaryote and eukaryote bioenergetic architecture. In giant prokaryotes, the cell interior is not complex, it is inert (2).

Finally, gene expression requires high concentrations of ribosomes, by far the most expensive cell component. By weight, *Escherichia coli* is 20% rRNA and 40% ribosomes, whereas 60% of yeast transcripts are rRNA, and half the mRNA encodes ribosomal protein (5). Lynch and Marinov neglect ribosomes. The energetic penalties they concede for moderately increased gene expression (1) are exacerbated for the most highly expressed genes in the cell—those for ribosomes, the enablers of gene expression. However, ribosomes are absent in their cost accounting.

Lynch and Marinov provide an account of ATP expenses that ignores the most costly component of the cell—ribosomes—and the source of eukaryotic ATP—mitochondria. When estimating cash flow within nations, the cost of government must be tallied, and tax income, too. Spending is constrained by income. Unlike governments, evolution does not tolerate deficit spending.

1 Lynch M, Marinov GK (2015) The bioenergetic costs of a gene. *Proc Natl Acad Sci USA* 112(51):15690–15695.
2 Lane N, Martin W (2010) The energetics of genome complexity. *Nature* 467(7318):929–934.
3 Allen JF (2015) Why chloroplasts and mitochondria retain their own genomes and genetic systems: Colocation for redox regulation of gene expression. *Proc Natl Acad Sci USA* 112(33):10231–10238.
4 Griese M, Lange C, Soppa J (2011) Ploidy in cyanobacteria. *FEMS Microbiol Lett* 323(2):124–131.
5 Kobayashi T (2011) Regulation of ribosomal RNA gene copy number and its role in modulating genome integrity and evolutionary adaptability in yeast. *Cell Mol Life Sci* 68(8):1395–1403.

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