

Asking endosymbionts to do an enzyme's job

Sriram G. Garg^a and William F. Martin^{a,1}

Zachar et al. (1) present a mathematical model for the origin of mitochondria in which the initial role of the mitochondrial symbiont was that of a food particle for its host. In their model, the bacterial endosymbiont can be freely acquired by a phagocytosing, amitochondriate host cell [an archezoan, in the words of Zachar et al. (1)] and can reproduce in the cytosol at a cost to the host. The core of their model is that symbionts can proliferate intracellularly and that during times of abundant external food supplies, this leads to the accumulation of food reserves (cytosolic bacteria) in the host's cytosol, while during leaner times, the host can harvest accrued food supply by digesting endosymbionts. From the standpoint of the host, the interaction with symbionts is akin to the interaction between humans and pigs, a kind of farming: "Farming is a form of bet hedging: the host applies different strategies in good and hard times to minimize its overall risk of extinction" (1). There are two problems with the Zachar et al. study.

First, the physiological benefit of evolving phagocytosis—the intracellular uptake of whole cells for food—over the standard prokaryotic heterotrophic feeding habit of importing small molecular weight metabolites, is only realized in the presence of mitochondria (2). That is one reason why primitively amitochondriate phagocytosing eukaryotes (Archezoa) have never been found (2) and why marine samples that Zachar et al. (1) offer as supporting metagenomic evidence for the existence of Archezoa or phagocytic Archaea, are unlikely to harbor such cells after all (3, 4).

The second problem is that Zachar et al. (1) employ intracellular bacteria to do an enzyme's job. Their model is founded on microbial "bet hedging" when

it comes to food supply. That is, natural selection can bring forth a trophic strategy in which cells use good times to accumulate food reserves that can be set aside, left untouched, and accessed on demand in bad times, thereby providing insurance against food supply extremes. Most microbes have been affected by, and have responded to, selection for food storage during evolution. The typical evolutionary response selected in nature is not endosymbiont farming, however, but expression and regulation of a handful of cytosolic enzymes for synthesis and mobilization of carbon and energy storage compounds (5–9).

Carbon and energy storage compounds are generally ubiquitous among archaea and bacteria, including photosynthesizers (6), typically consisting of glycogen, polyhydroxyalkanoates, or lipids (5–9). Eukaryotes are no different, routinely storing glycogen, lipids, or starch (10). Enzymatic control of intracellular carbon and energy reserve deposits requires fewer genes and is far more readily selected—and maintained—as a bet-hedging strategy for temporal resource allocation than acquiring and managing bacterial livestock in the cytosol. Prokaryotic and eukaryotic microbes bridge times of fickle food supply with enzymes for carbon and energy storage compound metabolism (5–10), a simple and robust reaction to limited resources in the microbial world. The model of Zachar et al. (1) explains the ubiquity of carbon and energy reserve compounds, not the singularity of mitochondria (2).

Acknowledgments

W.F.M. is supported in part by European Research Council Grant 666053 and Volkswagen Stiftung Grant 93046.

- 1 Zachar I, Szilágyi A, Számadó S, Szathmáry E (2018) Farming the mitochondrial ancestor as a model of endosymbiotic establishment by natural selection. *Proc Natl Acad Sci USA* 115:E1504–E1510.
- 2 Martin WF, Tielens AGM, Mentel M, Garg SG, Gould SB (2017) The physiology of phagocytosis in the context of mitochondrial origin. *Microbiol Mol Biol Rev* 81:e00008–e00017.
- 3 Sousa FL, Neukirchen S, Allen JF, Lane N, Martin WF (2016) Lokiarchaeon is hydrogen dependent. *Nat Microbiol* 1:16034.
- 4 Burns JA, Pittis AA, Kim E (2018) Gene-based predictive models of trophic modes suggest Asgard archaea are not phagocytotic. *Nat Ecol Evol* 2:697–704.
- 5 Wilkinson JF (1963) Carbon and energy storage in bacteria. *J Gen Microbiol* 32:171–176.

^aInstitute of Molecular Evolution, Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany

Author contributions: S.G.G. and W.F.M. wrote the paper.

The authors declare no conflict of interest.

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¹To whom correspondence should be addressed. Email: bill@hhu.de.

Published online May 3, 2018.

- 6 Stanier RY, Doudoroff M, Kunisawa R, Contopoulou R (1959) The role of organic substrates in bacterial photosynthesis. *Proc Natl Acad Sci USA* 45:1246–1260.
- 7 Bräsen C, Esser D, Rauch B, Siebers B (2014) Carbohydrate metabolism in Archaea: Current insights into unusual enzymes and pathways and their regulation. *Microbiol Mol Biol Rev* 78:89–175.
- 8 Hermann-Krauss C, et al. (2013) Archaeal production of polyhydroxyalkanoate (PHA) co- and terpolyesters from biodiesel industry-derived by-products. *Archaea* 2013:129268.
- 9 Spiekermann P, Rehm BHA, Kalscheuer R, Baumeister D, Steinbüchel A (1999) A sensitive, viable-colony staining method using Nile red for direct screening of bacteria that accumulate polyhydroxyalkanoic acids and other lipid storage compounds. *Arch Microbiol* 171:73–80.
- 10 Müller M, et al. (2012) Biochemistry and evolution of anaerobic energy metabolism in eukaryotes. *Microbiol Mol Biol Rev* 76:444–495.