PUBLISHED: 25 NOVEMBER 2016 | ARTICLE NUMBER: 16230 | DOI: 10.1038/NMICROBIOL.2016.230

Reply to 'Is LUCA a thermophilic progenote?'

Weiss *et al.* reply — In response to our recent paper[1], Gogarten and Deamer[2] write in with five paragraphs. They focus on traditional views concerning the nature of the last universal common ancestor (LUCA). We find the current exchange worthwhile in that it highlights several important differences in older and newer concepts concerning both LUCA and approaches to inference of its properties.

Their first paragraph, which summarizes some, but by no means all, virtues of submarine hydrothermal vents in the context of life's origin, requires no response, although John Baross[3], Mike Russell[4] and Everett Shock[5] can explain far better than we can how warmly the idea that life arose at hydrothermal vents was "welcomed"[2].

Gogarten and Deamer's second paragraph revisits older inferences about LUCA and the progenote that are based on the three-domain tree[6]. However, improved phylogenetic methods and better archaeal lineage sampling now deliver a different picture of domain relationships, called the two-domain tree, in which the archaeal partner at eukaryote origin arises from within the archaea, not as the sister of the archaea[7,8]. We can hardly be faulted that newer methods and data obtain the two-domain tree. Why is the issue of the three-domain verus two-domain tree important? It is this. Eukaryotes are derived from a single common ancestor that had both mitochondria and a very narrow sample of bacterial carbon and energy metabolism, demonstrating facultatively anaerobic chemoorganoheterotrophy[9]. Inferences about LUCA that trace eukaryotic properties to the first cells (the three-domain tree) always exclude most forms of microbial physiology — for example, nitrification, mineral oxidations, the knallgas reaction, sulfate reduction, methanogenesis, and so forth[5] — and can never recover traits such as anaerobic chemolithoautotrophy or the Wood–Ljungdahl pathway in LUCA for lack of such physiology in eukaryotes. Investigations of LUCA based on a three-domain approach to the problem can therefore not recover sets of genes similar to the ones we found using phylogenetic criteria that embrace the newer two-domain tree, which has been germane to our formulations of hydrothermal origins right from the beginning[10]. Gogarten and Deamer also lament in this paragraph that our results lead to an inference of LUCA that is not as complex as a free-living cell[2], or "half-alive", as we put it. We will return to this point in closing.

Their third paragraph deals with potential caveats of our method to address LUCA's properties. In our paper[1], under the subheading "Spelling out caveats and allowing for some LGT", we explained the issues concerning possible false positives and possible false negatives, but in greater depth and detail than Gogarten and Deamer[2]. We also mentioned examples[1]. Their comment just restates points that we made first.

The fourth paragraph complains that we do not obtain the same results as earlier studies that addressed the temperature at which LUCA lived, studies that were based upon the three-domain tree. Yes, that is correct. Our results really do differ from those in previous studies. In addition, the molecular thermometer papers they cite, which estimate growth temperatures from inferred GC content in selected regions of some genes, as modelled along the branches of the three-domain tree, would need to be repeated on the basis of more current archaeal lineage sampling along the branches of the two-domain tree[7,8].

In their fifth paragraph, Gogarten and Deamer criticize various aspects of the theory that life arose at hydrothermal vents, in particular the idea that the naturally chemiosmotic nature of alkaline hydrothermal vents could have been important for life's origin. The aspects of the hydrothermal vent theory that they criticize have been developed and discussed in many earlier papers by us and others[3,4,9–12]. In our recent genomic investigation study, we do not modify the theory, we merely find independent, genome-based evidence compatible with it. Hence, their critique applies to older papers and not ours[1], the findings of which are compatible with numerous aspects of some versions of the hydrothermal vent theory (the roles of metals, acetogenesis, methanogenesis, methyl groups, clostridia, methanogens, the acetyl-CoA pathway[11]), including the view that gradients[3] and chemiosmosis[4,9–12] were important at the origin of life. Can we be faulted that genomes deliver that result? Gogarten and Deamer[2] are particularly concerned that our study did not recover complete lipid biosynthesis, but we reported a number of membrane proteins within our dataset[1], indicating the presence of lipids in LUCA. Not all of the membrane proteins are drawn in Fig. 3, which summarizes physiology, but they are reported in Fig. 2 and elsewhere in the paper[1]. Yet, not only is lipid synthesis poorly represented, the majority of amino acid and nucleotide biosyntheses are missing too. As we wrote[1], lack of such essential functions among LUCA's gene set could indicate (1) that the missing genes unspectacularly underwent transdomain lateral gene transfer (LGT) post-LUCA, and hence were filtered out by our method, (2) that missing chemical components were provided by spontaneous abiotic syntheses during early Earth history, or (3) a combination thereof. LGT between the prokaryotic domains is both normal and natural[13] and all theories for the origin of cells, without exception, require abiotic syntheses; hence, we do not see any fundamental problems here. Their examples of universally present genes that are lacking from LUCA's list are not criticisms of our findings, rather they merely underscore what we wrote, namely that genes present in all genomes "can be affected by LGTs, such that only subsets of even universally present genes will also meet the domain monophyly criterion"[1].

Finally, Gogarten and Deamer[2] protest that our inference of LUCA contained "ribosomes, translation, genes, and a genetic code", offering that such a level of organization goes "far beyond what most would imagine as the first form of life"[2]. This is a very important comment. If the first form that Gogarten and Deamer consider to be alive lacks ribosomes, translation, genes and the genetic code, how can they possibly be worried that our version of LUCA, which has genes, ribosomes, the code, translation, exergonic carbon and energy metabolism, nitrogen fixation and many basics of cofactor biosyntheses, is only half-alive? Clearly, our version of early life[1] comes much closer to something that one might find in microbial culture collections (in freezers with acetogens and methanogens), than their version[2], which would not be deposited among archaea, bacteria, eukaryotes or viruses, but amidst organisms that lack ribosomes, the code, translation, and genes, and for lack of genes would have no heritable metabolism for either carbon, energy or nitrogen.

As the genetic code and some ribosomal proteins are universal to all cells, it seems inescapable that LUCA and the first forms of anything that we would call alive possessed genes. Our study is based on genes. It is clearly not possible to test the concept of gene-lacking life forms[2] using genomic data. In closing, they ask for suggestions for how to test the idea that life arose at hydrothermal vents. Laboratory[12,14] and field[15] investigations have already been reported and, looking at the matter openly, our contribution is a test of the hypothesis as it relates to genomes[1]. In summary, Gogarten and Deamer[2] summarize their views concerning LUCA and we have welcomed this opportunity to summarize ours. ❐

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