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Ten good reasons not to exclude giruses from the evolutionary picture

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In their recent review article (Ten reasons to exclude viruses from the tree of life. *Nature Rev. Microbiol.* **7**, 306–311 (2009))[1], Moreira and López-García present a conservative, dogmatic and somewhat diminishing view of viruses and their role through evolution. According to them, everything is now understood, which does not leave much hope for the future generation of scientists to significantly modify today's dominant scenario for the origin of life on our planet: the 'tree of life' is firmly planted (although not yet rooted on any scientific ground, as far as we know) and no virus will ever be part of it. Fortunately, scientific history has shown us repeatedly that such a peremptory stance, the 'we know it all' attitude, is often followed (and ridiculed) by a brutal paradigm shift, as defined by Thomas Kuhn[2]. We think, with others, that the unique features of Mimivirus[3–6], and the renovated interest it has brought to the study of other giant viruses, should trigger both a reappraisal of the concept of 'viruses' and of the role they might have had in the early evolution of eukaryotes[7]. To encourage younger evolutionists to challenge the traditional view, here are ten good reasons to disagree with Moreira and López-García.

First, committees do not rule scientific truth. We were amazed to see that Moreira and López-García cited the acknowledgment of the International Committee on Taxonomy of Viruses (ICTV) in 2000 that viruses are not alive as a valid argument in their article. Historians of science could list innumerable cases of venerable committees and academies enouncing scientific 'truths' that were in general short-lived. To the defence of our ICTV colleagues, it is worth noting that their strong position was taken before the first publication on Mimivirus, which prompted many virologists to look at large DNA viruses from a different evolutionary perspective[7–9].

Second, if viruses are not alive, what about parasitic bacteria and spores? To exacerbate the difference between viruses and cellular organisms, the authors focused on the 'virion' state of minimal viruses (such as RNA viruses) compared with 'free living' bacteria in a metabolically active state. This is not a valid comparison. Virions should be compared with bacterial spores that are metabolically inactive. Admittedly, there is much less phenotypic difference here. In this conceptual debate, it is only fair to compare equivalent states, such as the replicating stage of a giant virus with that of an obligatory parasitic bacterium. Yet, despite their inability to replicate outside a host, no one ever seems to dispute the fact that *Rickettsia*, *Buchnera* or *Carsonella ruddii*, which has a 160 kb genome lacking many genes thought to be to be essential in bacteria[10], are living entities. At some point, we will have to face the paradox that even though 'life' is an all-or-nothing concept, 'living' organisms span a continuum of autonomy and complexity, in which large DNA viruses now largely overlap the smallest bacteria.

Third, viruses are polyphyletic, but only 'girus' should be discussed in this situation. One of the lessons we immediately drew from the discovery of Mimivirus was that the word virus does not adequately reflect the diversity in size, structure and physiology of the 'objects' it collectively refers to. The modern signification of the word virus was inherited from their discovery as 'filtering infectious agents', and therefore focused on the virus particles. Amazingly, we are still using this word that was coined more than a century ago, totally disregarding the diversity of replication strategies subsequently found in the viral world, as now summarized in Baltimore's classification. Following the characterization of Mimivirus, we proposed the new term girus to emphasize the unique property (and perhaps evolutionary origin) of large DNA viruses[9]. Asking whether viruses as a whole should enter the tree of life has no scientific meaning. Asking if ancestral giruses might not be part of the

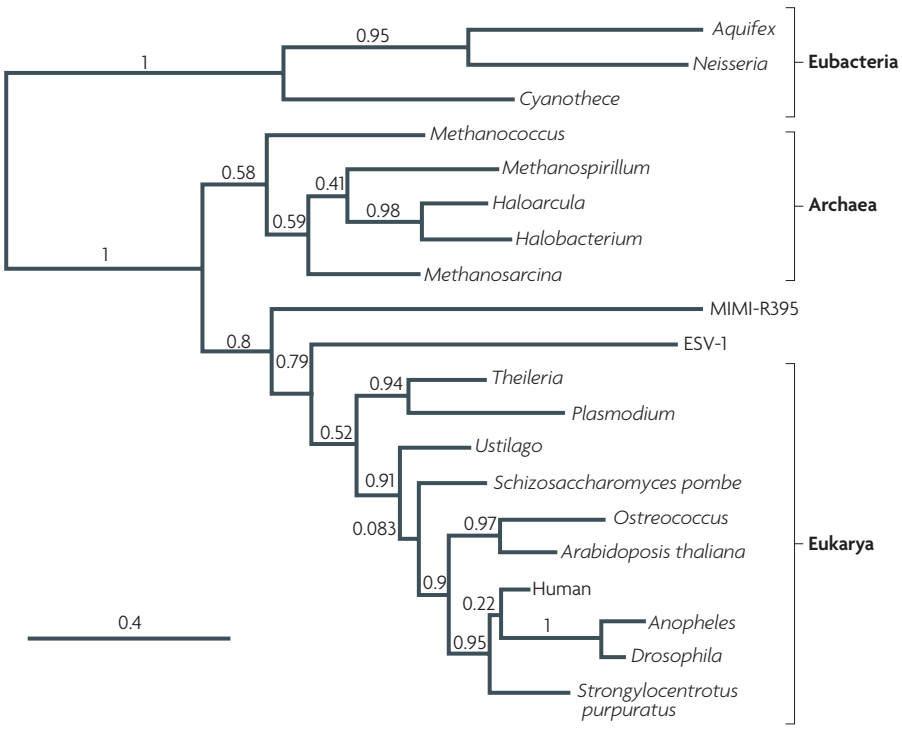

Figure 1 | **Giruses in the tree of life: between Eukarya and Archaea.** Despite high bootstrap values, a common criticism of the phylogenetic trees built from various mimivirus genes is the long branches that connect them to the tree trunk owing to their low similarity with cellular homologues. We identified the clamp loader proteins as an alternative set of sequences that exhibit minimal divergence (>25% identity over more than 250 residues across the 3 domains of life) and are present in a few large eukaryotic viruses, including Mimivirus and *Ectocarpus siliculosus* virus-1 (ESV-1). As shown here, robust phylogenetic trees that encompass the three domains of life can be made from the reliable multiple alignment (194 positions retained) of Mimivirus clamp loader (R395) with its most similar homologues in cellular organisms. The server at www.phylogeny.fr was used with the default parameters (rooting at mid-point).

underground reticulated roots of a 'forest of life' is a legitimate question.

Fourth, giruses are no more gene robbers than bacteria. In their second figure, Moreira and López-García[1] once more propagate the urban legend that Mimivirus is a gene robber. This figure is misleading. First, it fails to acknowledge that 86% of Mimivirus genes do not resemble any cellular genes, as it is the case for other giruses. To us, the existence of such a genomic 'dark matter' of unexplained origin is a strong warning that today's dominant picture of the evolutionary origin of life might be fundamentally incomplete (interestingly, cosmologists have a similar problem). We cannot have it both ways: on one hand claiming that viruses keep acquiring their genes from cells, but on the other hand observing that most of them lack cellular homologues. Traditional evolutionists would claim that the similarity was erased by the fast evolution rate of viruses. We have shown that such a scenario does not hold for giruses[11,12]. We found that proponents of the 'gene robbing' theory tend to be less stringent (in terms of branch length and bootstrap values) in identifying horizontal gene transfers in their own work[13], than in accepting our evidence of deep Mimivirus gene ancestry[3,5] (FIG. 1). The predominant host origin of girus genes was recently dismissed by its former proponents[13,14].

To briefly summarize additional points, fifth, viruses have diverse evolutionary origins, and discussing them all at once does not make sense. Sixth, in the world of viruses, giruses such as Mimivirus have their own evolutionary history. Seventh, their origin might have predated the divergence of today's three cellular domains, readily explaining the presence of bacterial-like, archaeal-like and eukarya-like genes in their genome[7]. Eighth, reductive evolution is an evolutionary process that is commonly found in parasites. This suggests that girus ancestors were endowed with more cell-like properties, perhaps enough to be considered alive[7]. Ninth, not confronting the disturbing fact that most girus genes might not have originated from one of today's three cellular domains only helps revive the spectrum of intelligent design. Finally, tenth, giruses might not readily fit into today's tree of life simply because its picture (in particular its root) does not adequately represent the evolutionary relationship of living organisms on our planet[15].

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