How *Acanthamoeba polyphaga* Mimivirus Changed Virology

**Abstract:**

 In 2003, researchers Philipe Colson, et al discovered a peculiar virus infecting amoeba and presented their groundbreaking discovery in “Mimivirus: Leading the Way in the Discovery of Giant Viruses of Amoebae.” The virus was bigger than any virus found before and much bigger than the smallest bacteria. This virus is *Acanthamoeba polyphaga* mimivirus, or AMPV, and it set the stage for the discovery of several species that scientists now call giant viruses. The question of what constitutes a living organism creates a lively debate in a room of microbiologists and nobody can seem to come to an agreement on whether viruses should be considered alive.

 Giant viruses further muddy the waters of the debate, as they possess features that makes their complexity rival bacteria and some eukaryotes. The discovery has also revived a few hypotheses that center viruses at the base of our evolutionary tree. As smaller bacteria and larger viruses are discovered, microbiologists may need to revisit these questions about what qualifies life and the origin of complex species again, but with mimivirus as their starting point.

**Introduction:**

 When trying to determine if an object is living or not, scientists may consider a few criteria. Most simply, some scientists consider an organism living if they can reproduce on their own, if they are enclosed in a membrane that clearly separates the organism from its environment, and if they require/use energy. Viruses can replicate their genome and produce copies of themselves, but they require a host because they lack ribosomes. Viruses have a protein coat called a capsid which contains their genetic material, but they do not have cell membranes like other organisms do. Finally, viruses use energy when they are in a host cell, but if they are not currently infecting a cell, they are in a dormant phase in which they do not use or require energy. Broken down like this, it seems difficult to understand why there is a debate at all, but let’s explore some of the reasons microbiologists may disagree with these claims or criteria as a whole.

 Some may say that all living creatures rely on other organisms for their survival and reproductive success, so instead of labeling viruses as non-living, they may think “obligate intracellular parasite” is a more apt characterization. Though viruses do not have a cell wall or membrane, some may point out that a capsid does a similar job by clearly separating the environment from the viral genome, allows the virus to interact with host cells, and it protects the genome from environmental hazards. Further, there are some obligate intracellular parasitic bacteria and eukaryotes that only use energy when they are in a host cell. These are just a few reasons why drawing a hard line in the sand declaring viruses living or nonliving is difficult for microbiologists, but giant viruses are making the decision even harder.

**Recent Progress**

There are three main hypotheses concerning how viruses fit into evolutionary history: the progressive/escape hypothesis, the regressive hypothesis, and the virus-first hypothesis (Wessner 2010). The progressive hypothesis states that viruses arose from mobile genetic elements gaining the ability to enter and exit cells. The progressive hypothesis is supported by the similarity between HIV, a retrovirus, and retrotransposons in eukaryotic cells. The second hypothesis is the regressive hypothesis, which postulates that as viruses evolved to be parasites, they lost genetic information along the way. Perhaps they used to be a more complex organism, like a bacteria or eukaryote, but as they evolved, they lost unnecessary genetic complexities along the way. The giant viruses discussed in this paper support the regressive hypothesis, as they could serve as the “missing link” between the modern-day small viruses and the theorized complex ancestor of the modern virus. The last hypothesis is the virus-first hypothesis. This hypothesis is fundamentally different from the other two as it proposes that viruses predate cellular life, and viruses gave rise to all of the cellular life on earth. Scientists have an issue with the virus-first hypothesis because modern day viruses cannot replicate on their own, so how could viruses give rise to the three domains of life: archaea, bacteria, and eukarya?

 The research that Colson and his team conducted with mimivirus and the subsequent discovery of other giant viruses complicates questions about what constitutes being a living organism and our hypotheses about viral evolution. Giant viruses are different from smaller viruses in a few important ways; giant viruses can become infected by virophages (other viruses), they have their own mobile DNA elements (transpovirons), and they have evolved a defense mechanism against the aforementioned virophages – something virologists call the mimivirus virophage resistance element (Colson 2017). They are structurally different from their smaller cousins, too. Viruses are typically only enclosed in a protein coating called a capsid, but mimivirus has fibrils covering their capsid. These fibrils are unique to mimivirus, provide protection to the virus’s genome, and allow it to attach to amoebae, bacteria, arthropods, and fungi (Colson, 2017). Mimivirus possesses another unique cell-surface feature, a star-shaped area without fibrils that scientists have named the stargate. Mimivirus and other giant viruses have unique genes that encode for translation factors, aminoacyl-tRNA synthetases, and proteins involved in nucleotide synthesis, amino acid metabolism, DNA repair, protein folding, and protein modification (Colson 2017).

 Since the discovery of the *Mimiviridae* family, a second giant virus family has been established: *Marseilleviridae.* There are also a few proposed giant virus families that need further research. There has also been a phylogenetic linkage established between giant viruses that infect amoebae with a group of double-stranded DNA viruses called nucleocytoplasmic large DNA viruses (Colson 2017). Due to their shared conserved regions, there was a movement to combine giant viruses of amoebae with nucleocytoplasmic large DNA viruses, but the authors of this research article argue that there are distinct differences that should keep them separate. Additionally, the replication cycle of AMPV differs from other viruses. Like all known viruses, AMPV replicates within a host cell. Unlike other viruses, there is evidence that AMPV doesn’t completely rely on the host cell to replicate their genome. AMPV has been shown to insert its genome into the amoebal cytoplasm through its stargate that establishes a replicative center, termed a viral factory. Research has not been conclusive on how and to what extent amoebal nuclear factors are involved in the replication of AMPV, but they have observed that the amoebal nucleus decreases nearly twofold during the process (Colson 2017).

**Discussion**

These viruses have complexities that rival some bacteria. The smallest known bacterial genome, belonging to *Carsonella ruddii*, is a mere 182 genes (Ball 2006). The AMPV strain has a staggering 979 genes, dwarfing many of the simplest bacteria. For reference, viral genome size typically ranges from 1,760 base pairs on the small side (porcine circovirus) to 170,000 base pairs on the large side (Epstein-Barr virus). Mimivirus clocks in at 1,200,000 base pairs (Milo 2016). Previously, it was thought that 300 genes was the minimum requirement for a living cell, but these discoveries complicate our view of the world around us (Alberts 2002). Since the discovery of AMPV, approximately 100 other strains of mimivirus have been found and other giant viruses have been discovered as well. Now that virologists know giant viruses are out there, it is safe to assume more will be discovered and potentially complicate the picture further. All the current research points to giant viruses being vastly more complex than any smaller virus and even some bacteria and eukaryotes, but most genes of giant viruses still haven’t been thoroughly researched. Further research is required to fully elucidate the significance of this discovery.

On the human side of things, giant viruses have been implicated in human infection. Mimivirus has been found in patients with pneumonia and Marseillevirus was first discovered in the stool of a healthy individual from Senegal. Later, Marsiellevirus was implicated in blood and lymphoid tissue infections (Colson 2017). The more scientists discover about giant viruses, the more questions seem to arise. As Colson proposed, if these newly discovered viruses don’t possess ribosomes but rival many bacteria and some eukaryotes in genetic complexity, scientists should potentially reconsider the differentiation between viruses and bacteria. If further research shows that AMPV doesn’t rely completely on the host cell’s machinery to replicate, that might add more weight to the potential of viruses being reclassified as living organisms. Further, our expanding knowledge of giant viruses may influence evolutionary biologists and virologists research into the evolution of cellular life. Giant viruses may become a new research interest for emerging disease experts as their propensity to cause the next human epidemic is currently up for debate. Many research questions remain, big and small, and further investigation of giant viruses could shake up the field of virology, evolutionary biology, and human pathology.

References

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