Obelisks – Newly discovered virus-like particles

Researchers from Stanford have reported the discovery of new biological entities that they have called "obelisks", based on their shape. These small particles are circular single-stranded RNA molecules of around 1,000 bases that contain one or two genes and self-organize into a rod-like structure (*Zheludev et al., BioRxiv 2024*).

Craig Venter is one of the pioneers of synthetic genomics (*Venter et al., Cell 2023*). He was the first to manipulate the simplest cells to see what was essential for life. In 1995, he published the complete genome of Mycoplasma, the simplest cell with autonomous growth, which has 525 genes (*Fraser et al., Science 1995*). In 2016, he inserted a synthetic DNA molecule with 531 Kb into a mycoplasma, from which he had previously removed its nucleic acid. It had only 473 genes, which are essential for retaining the ability to survive and replicate autonomously (*Hutchison et al., Science, 2016*). Although the function of many of these genes remains unknown, only 206 genes would be essential for life.

Viruses are not living organisms, since they lack the major features that define a living being, such as independence, metabolism, information retained and transmitted to descents, and vital cycle (Table 1). Viruses are parasites as they need to infect cells, either Bacteria, Archaea, or Eukarya, to complete their biological cycle. Without a host, there are no viruses. However, there are far more viruses than cells, being estimates of 10^{32} on the planet. They can be found in every conceivable habitat. By infecting and manipulating their hosts, viruses have probably influenced the evolutionary trajectories of all life.

Table 1. Main characteristics of the living being.

1. Independence. Membrane. Compartments.
2. Metabolism. Capture of matter and energy. Increased internal complexity at the cost of increased external entropy
3. Information retained and evolution. Step to descent and movement. Replication and adaptive capacity
4. Life cycle. To be born, to grow and to die. Vital clock

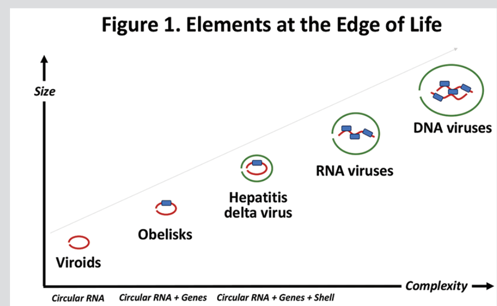

Figure 1. *Elements at the edge of life.*

There are more than 80 different families of viruses. Although many viruses contain DNA as genetic material, more than 200 viruses, including those that cause flu, AIDS, Ebola, COVID-19, and hepatitis C bypass DNA, having genomes composed only of RNA.

Viroids are smaller and simpler than viruses. They are RNA molecules that can self-cleave and re-ligate their genome as part of the replication cycle. This enzymatic activity behavior by a nucleic acid is acknowledged as ribozyme. Viroid genomes do not encode any proteins at all.

They were first discovered in the 1970s when some were found to cause diseases in plants. Soon scientists discovered a similar element that can cause hepatitis in humans, the hepatitis delta virus (HDV). During the past 5 years, several studies have reported viroid-like circular RNA genomes amid databases of sequences from animals, fungi, and bacteria.

The HDV is a unique defective virus. HDV only exists associated with the hepatitis B virus, which provides its envelope, as a parasite of another parasite (*Asselah and Rizzetto. N Engl J Med 2023*). HDV contains a short RNA molecule of 1,700 bases. It does not have its own replicative enzyme but uses a polymerase from the infected hepatocyte. Its RNA molecule shows autocatalytic or ribozyme activity, which is essential for viral replication. In addition, it is the template for the synthesis of a single viral protein, the delta antigen.

Obelisks, the newly discovered biological entities, fall somewhere between viruses and viroids (Fig. 1). They are more like RNA plasmids, which are genetic elements that reside inside bacteria and transfer between them. Like viroids, obelisks have a circular single-stranded RNA genome but smaller (of around 1,000 bases) and no protein coat. However, like viruses, their genomes contain genes that codify proteins. All 30,000 obelisks described so far in the gut and mouth of humans by Stanford's team encode a single major protein known as obulin, and many encode a second smaller obulin. These proteins do not make a shell. Of note, obulins do not share any homology with any other known protein. Hence, there is no clue about their function.

Obelisks are not rare and must be widespread across multiple niches. They were detected in around 7% microbiome datasets from the human gut and 50% of datasets from the human mouth. Different obelisk types were found in different body sites and in distinct donors. Long-term data revealed that people can harbor a single obelisk type for around a year.

Bacteria and fungi are likely hosts of obelisks. At this time, it is unclear whether obelisks may be parasitic and harm cells or they may be beneficial. Hosts may have evolved elaborating defense mechanisms against obelisks or else actively recruit them to gain some unsuspected advantage. If obelisks modulate the human microbiome, this may in turn have implications for human health – they may even have therapeutic potential.

Alternatively, obelisks may cause neither harm nor benefit to their microbial host or humans. Instead, they may simply exist as stealthy evolutionary passengers, silently, and endlessly replicating, like the original "*selfish gene*" (*Dawkins R. 1976*).

Experiments with obelisks are planned and could reveal truths about the origin of life itself. Because viroids and their relatives are small, simple, and have the capacity to self-replicate, they could be the precursors of all life on Earth. One big question is whether viruses evolved from increasingly complex viroids and obelisks or emerged first and then degenerated into these simpler structures (*Penni E. Science 2024*). The long-term evolution of viruses on Earth starts to slowly emerge.

Vicente Soriano[1], Víctor Moreno-Torres[1,2], and Octavio Corral[1]
[1]UNIR Health Sciences School; [2]Puerta de Hierro University Hospital. Madrid, Spain

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The origin of the four major focus of HTLV-1 in Latin America

HTLV-1 was discovered in 1980 as the first human retrovirus. As zoonosis, HTLV-1 derives from jumps to humans from simian T-lymphotropic virus naturally infecting monkeys in Central and Western Sub-Saharan Africa for thousands of years. Molecular clock study estimates an ancestor for all human HTLV-1s around 30,000-40,000 years ago[1].

As expected, Africa accounts for the largest number of HTLV-1 infections worldwide[2]. However, Latin America is the second region endemic for HTLV-1 globally. As shown in figure 1, four areas of high HTLV-1 prevalence can be recognized, namely, at the Caribbean basin, Brazil, Peru, and along the Andes mountains. Phylogenetic studies have examined viral sequences from isolates in all these regions, including the exam of older mummies[3-5]. Based on these data, a reconstruction of the earliest introduction and dissemination of HTLV-1 in America can be postulated.

From its origin in West and Central Africa, HTLV-1 was introduced into Central Asia. During the last Glaciation, human populations migrated through the Bering Strait 35,000-15,000 years ago and introduced HTLV-1 in the Americas. The presence of HTLV-1 in aboriginal populations from Kamchatka at one side of the Bering Strait and in native skimos and Amerindians on the other side confirms this hypothesis[6]. During the warming period that followed, migrations to the South occurred along the long Andean mountains range. This movement carried HTLV-1 south and accounts for the presence of HTLV-1 across distinct native Amerindian tribes from Colombia to Chile[7-11].

During the XVI to XIX centuries, a second wave of HTLV-1 arrived to the Caribbean basin and Brazil during the colonial times along with the slaves taken in West Africa mostly by Portuguese and British[12-15]. More recently, during the XX century, migrants from Japanese endemic southern areas to Peru and Brazil established a new settlement of HTLV-1 in Latin America.

In Brazil and Peru, both highly endemic countries for HTLV-1 infection, two major distinct sources of the virus can be recognized. In the Amazon tribes of inner Brazil, the ancient HTLV-1 variants infect Amerindians. In the Brazilian coast, HTLV-1 variants that arrived with the slavery trade predominate by far. The arrival of Japanese to large coastal cities of Brazil during the last century added a new variant. In Peru, the newly arrived Japanese HTLV-1 variant has been added to the ongoing circulation of ancient HTLV-1 introduced along the Andean populations thousands of years ago.

Vicente Soriano[1] and José Manuel Ramos[2]
[1]UNIR Health Sciences School and Medical Center, Madrid;
[2]Miguel Hernández University of Elche, Alicante. Spain