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Giant viruses at the core of microscopic wars with global impacts

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The unicellular eukaryotes (also called protists) that inhabit the contemporary oceans have large impacts on major biogeochemical cycles. Populations of oceanic protists are to a large extent regulated by their viral parasites, especially nucleocytoplasmic large DNA viruses (NCLDVs). NCLDVs can themselves be the prey of smaller viruses called virophages and can also be infected by transposable elements termed transpovirons. These entangled parasitisms have fostered the emergence of sophisticated infection and defence strategies. In addition persistent contact has facilitated the exchange of genes between different parties. Recent advances shed light on the strategies that govern such microbial wars. Endogenous virophage-like elements found in the genome of a marine alga could for instance provide the host acquired immunity against NCLDVs. In return, it was recently speculated that virophage sequences can be hijacked by NCLDVs and used as genetic weapons against virophages.

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Introduction

Viruses are ubiquitous in ecosystems and have a wide impact over their host populations. An apparently monophyletic order of highly complex double-stranded DNA viruses are major parasites of a variety of eukaryotes and are named after some of their key features as to nucleocytoplasmic large DNA viruses (NCLDV, proposed order Megavirales) [1,2]. They comprise by far the largest known viruses with genomes scaling from a hundred kilobases (kb) to 2.5 megabases [3], including specimens with capsids of up to 1.5 μm in length [4].

Some NCLDV families are themselves being preyed upon by much smaller satellite viruses termed virophages [5]. Virophage are double-stranded DNA viruses that hijack the NCLDV replication machinery for their own multiplication. Another example of NCLDV parasites is the group of transposable elements transpovirons that can colonize NCLDV genomes with potential deleterious effects [6].

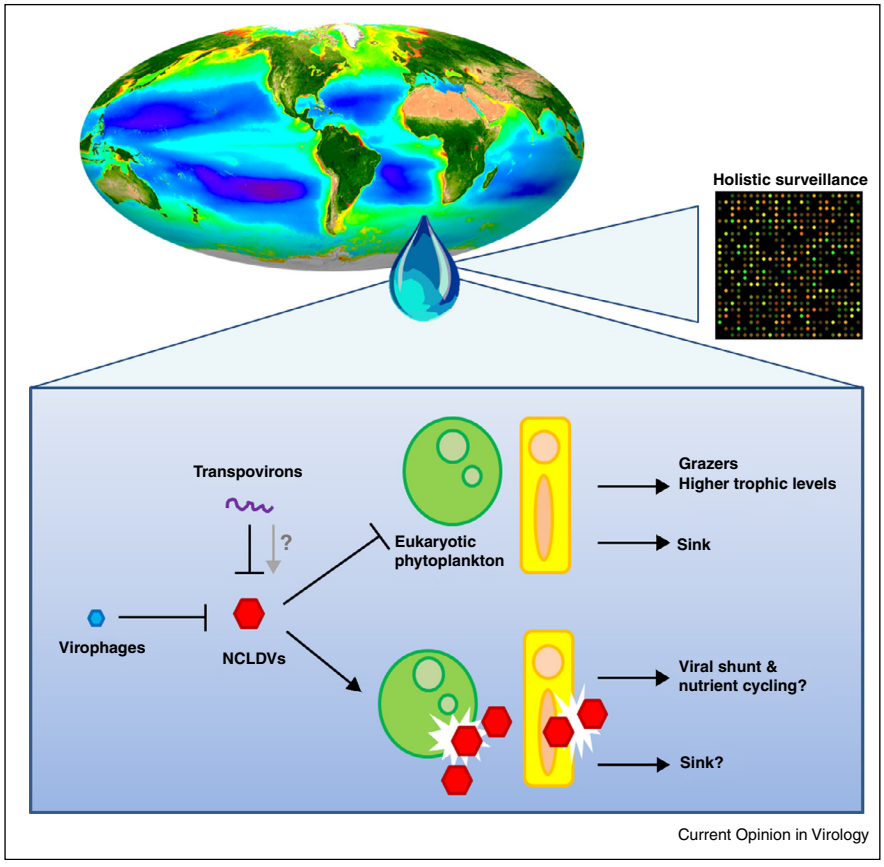
The terms of these entangled and chained parasitisms are just beginning to be addressed as virophages and transpovirons have only been discovered in 2008 and 2012, respectively [5,6]. In addition, several new families of Megavirales of extreme size and extended gene repertoire are continuously being reported since the discovery of mimivirus in 2004 [7], a NCLDV with exceptional genome size (nearly twice that of any other known virus at the time) that fostered the hunt for giant viruses. NCLDV and virophages are abundant in a variety of ecosystems as attested by their presence in multiple metagenomics samples, especially from the marine environment [8,9••,10••]. Therefore, the characterization of the molecular and genetic battles that agitate the relationships between transpovirons, virophages, NCLDVs and their host is a boiling topic.

Especially at sea where all these tiny bugs meet and eat: viruses are the most abundant entities in the marine environment with concentrations that reach 10^{10} ml^{-1} in surface waters and their impact on the composition of microbial communities and nutrient cycling is paramount [11]. Because marine ecosystems are essential in the regulation of biogeochemical cycles and climate [12], this short review aims to emphasize on the NCLDV-centered marine microbial battles and their possible impacts on the ecosystem (Figure 1).

NCLDV–host interactions

Altogether, the different families that constitute the NCLDV clade have wide host spectra including eukaryotic organisms as diverse as various protists, human and probably plants (see [13,14]). NCLDVs are especially abundant in marine ecosystems with an estimated 10^4–10^5 genomes ml^{-1} in the photic zone [9••]. Within marine systems, the NCLDVs can establish contact with their

Figure 1



The world of marine NCLDVs. Top left panel: SeaWiFS (Sea-viewing Wide Field-of-view Sensor) image showing average chlorophyll concentration on Earth. High chlorophyll regions in the oceans (red, yellow, and green pixels) are the most productive over time owing to dense phytoplankton blooms; top right panel: image of DNA microarray symbolizing the genetic analysis of environmental samples. Metagenomic surveys will enable to identify new partners and relationships that can then be monitored for instance using microarray and put in connection with a range of metadata collected over time course; bottom panel: schematic view of the virophage/transpoviron/NCLDV/eukaryote interactions and putative outputs to the ecosystem.

host through passive dispersion and diffusion in water masses [15]. Recently, zooplankton including copepods and other crustaceans were also found to serve as vectors that can transmit NCLDVs between marine algae [16]. NCLDVs spreading strategy unexpectedly extends beyond the aquatic environment. For instance, aerosolised NCLDVs particles were detected in atmospheric samples collected above the oceans. Under specific meteorological conditions, this could allow dispersal and infectivity over hundreds of kilometers [17••].

The proposed order Megavirales comprises viruses with different lifestyles [18]. Upon contact between Mimiviridae and their hosts, adhesion to glycans at the surface of amoebae cells is mediated by the dense glycoprotein fibril layer of the virus capsid [19]. The entire virus particle is then engulfed via phagocytosis [20]. On the other hand, infection of the algal Chlorella virus PBCV-1 (Phycodnaviridae) follows a bacteriophage-like mechanism. The virus attaches to receptors on the surface of the green alga by a unique vertex and digests the cell wall at the contact point, before releasing its DNA and virion-associated proteins inside the cell, leaving outside the empty capsid [21]. There is a diversity of entry modes even among phycodnaviruses: some enter their host through endocytosis or envelope fusion [22] while the mechanism is unknown for others.

Many NCLDVs are thought to accomplish replication and transcription at least partially within host nuclei (see [23]). The mechanisms enabling the trafficking of large capsids or long genomes from the cell periphery to the host nucleus are still unclear and controversial, considering the obstacles formed by the highly viscous cytosol, the cytoskeleton network and the endoplasmic reticulum [24]. The mechanisms of translocation of very large genomes within the nucleus also remain mysterious considering the apparently undersized diameter of nuclear