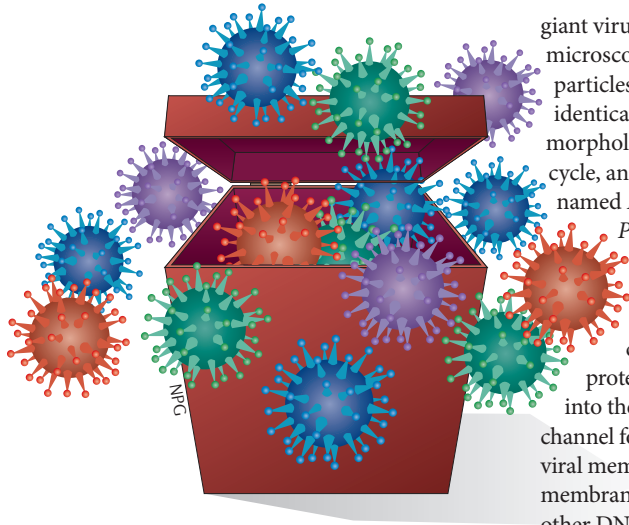


 VIRAL BIOLOGY

# Pandora's box goes viral



The discovery of the first giant DNA virus 10 years ago (Mimivirus of the family *Megaviridae*), which resembles parasitic bacteria in terms of its physical size and genomic complexity, challenged our preconceptions of the distinction between viruses and cellular life forms. Philippe *et al.* now report the discovery of two new giant viruses that are morphologically and phylogenetically distinct from members of *Megaviridae*, with genomes that are up to twice the size.

The authors examined sediments from aquatic environments in which the *Acanthamoeba* sp. host of giant viruses is most prevalent. Two samples demonstrated the intracellular multiplication of unusually large, antibiotic-insensitive particles that had strong lytic activity, indicative of

giant viruses. Optical and electron microscopy demonstrated that the particles from both samples had an identical micrometre-sized ovoid morphology and a lytic replication cycle, and they were subsequently named *Pandoravirus salinus* and *Pandoravirus dulcis*.

Similarly to Mimivirus, these pandoraviruses are internalized into phagocytic vacuoles, and viral proteins and DNA are released into the cytoplasm through a channel formed by fusion of the inner viral membrane with the vacuolar membrane. However, unlike for other DNA viruses, synthesis of the pandoravirus envelope and packaging of the internal compartment occur simultaneously, in an atypical manner referred to as 'knitting'. Both viruses also exhibit hallmarks of viral infection, such as eventual destruction of host nuclei, with subsequent cell lysis and the release of progeny virions.

Genome sequencing revealed that the pandoravirus genomes were more GC-rich and up to twice as large as those from other giant viruses. The *P. salinus* genome is 2.47 Mb and contains 2,556 putative protein-coding sequences (CDSs), whereas the 1.91 Mb genome of *P. dulcis* consists of a subset of the *P. salinus* genomic content. Thus, the larger genome was selected for further study.

Strikingly, only 17 of the 2,556 *P. salinus* CDSs had homology with

known *Megaviridae* genes, and 93% of the CDSs did not resemble any known genes. Although the genome encoded several DNA-processing enzymes, more than half the core genes of large double-stranded DNA viruses were absent, particularly those considered to be essential for DNA replication. Furthermore, unlike all large cytoplasmic DNA viruses (including those from *Megaviridae*), the genome contained several spliceosomal introns, whereas genes encoding the transcriptional machinery were absent. Together, these data suggest that pandoraviruses are heavily dependent on host nuclear functions, at least during the early stages of the viral life cycle.

The authors note that pandoravirus-like particles had been observed previously, but owing to their enormous size, they were not expected to be viruses. These remarkable findings reinforce the notion that our understanding of the breadth of microbial diversity is far from complete, and considering that the genomic size of pandoraviruses exceeds that of some eukaryotic microorganisms, the upper limits of the viral world continue to surpass our expectations.

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**ORIGINAL RESEARCH PAPER** Philippe, N. *et al.* Pandoraviruses: amoeba viruses with genomes up to 2.5 Mb reaching that of parasitic eukaryotes. *Science* **341**, 281–286 (2013)