MICROBIOLOGY

Ever-Bigger Viruses Shake Tree of Life

"It's like finding a sasquatch," says Elodie Ghedin, a virologist at the University of Pittsburgh in Pennsylvania. That's one of the amazed reactions to the discovery, reported on page 281, of two new viruses with by far the largest genomes ever seen in a virus, including one that's bigger than the genomes of some parasitic eukaryotes. The virologists in France who unearthed the massive viruses—the biggest one is 1 micron long, a hundred times the size of many viruses—suggest that their finds challenge the long-standing view that viruses don't qualify as life.

"It is clear that the paradigm that viruses have small genomes and are relatively simple in comparison to cellular life has been overturned," says Curtis Suttle, a virologist at the University of British Columbia in Vancouver. The genome of one of the viruses is 1.91 million DNA bases long, while the other runs 2.47 million bases. That dwarfs some bacterial genomes and edges into the eukaryotic realm (see chart).

Jean-Michel Claverie and Chantal Abergel from CNRS, the French national research agency, at Aix-Marseille University in France, and their colleagues have dubbed the new viruses pandoraviruses because of their amphora shape and the surprises they may portend. They have strikingly different genes and physical appearances from other viruses. The finding "expands our view of the virus world," Ghedin says.

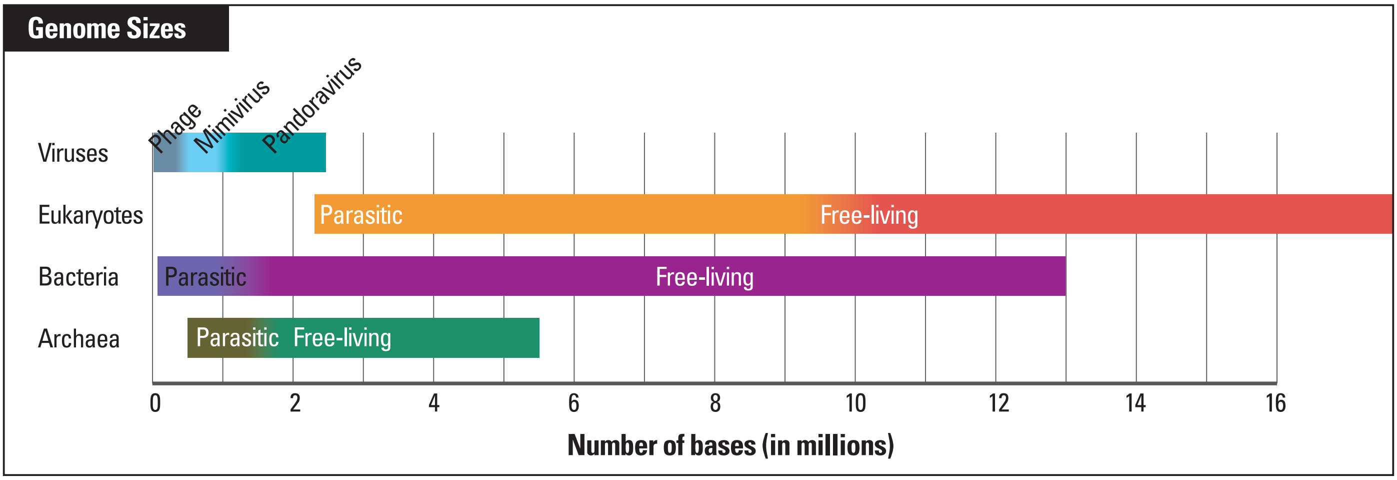
After their late 19th century discovery, viruses were quickly demoted to inert particles, too simple to belong to the realm of the living. Considered little more than a protein package of genetic material with no metabolic capabilities, viruses must get inside a cell and coax their host to replicate them, because they can't make their own proteins.

A decade ago, the discovery in an amoeba of a virus that rivals the size of a small bacterium prompted a rethinking of how viruses originated and what they could do. Didier Raoult, a microbiologist at the University of the Mediterranean in Marseille; Claverie; and their colleagues sequenced the genome of mimivirus, for "microbe mimicking virus." Its 1.18 million bases contained more than 900 putative genes, some closely resembling genes in nonviruses that are involved in protein production (*Science* 28 March 2003, p. 2033; 19 November 2004, p. 1344).

Mimivirus could have acquired those genes from its cellular hosts, but the mimivirus genes are so different from those of the host amoeba and other cells that Raoult and Claverie instead proposed that mimivirus descended from a free-living cell that gradually lost most of its other genes as it became a parasite. That mimivirus precursor, they suggested, represented a previously unknown branch of life, one predating the emergence of the three major branches, or domains, of life—bacteria, archaea, and eukaryotes.

This theory remains controversial, but it has motivated Claverie to keep hunting for viral giants. "According to this scenario, looking for even bigger viruses with bigger genomes was a way to go back in time, to take a closer, earlier look at this postulated ancestor," he says. He and other researchers have since come across several other giant viruses, including *Megavirus chilensis*, at 1.25 million bases the previous viral genome record-holder. It has many of the same genes as mimivirus, plus a few more, and seems to represent an intermediate step between a free-living ancestor and mimivirus

Now, scans of the water and sediment samples that Claverie, Abergel, and other lab members gather whenever they travel have yielded the pandoraviruses. (The researchers inoculate amoeba with the samples to see if any viruses replicate and burst out). The one with the smaller genome came from mud in an Australian pond, while the new king of the viral genomes was in coastal sediments collected off Chile. "The fact that two of them were found almost simultaneously from very distant locations either indicates we were incredibly lucky or that they are not rare," Claverie says. "They are probably everywhere."



Because of their size, the pandoraviruses appeared bacterialike at first. But using light and electron microscopy, the French group followed the newfound entities through a replication cycle, which proved viruslike. Instead of dividing in two like a typical bacterium or cell, they generated hundreds or more new viral particles, Claverie's team reports. Both pandoraviruses lack genes for energy production and can't actually produce a protein on their own, fulfilling the definition of virus. "The authors seem to have gone the proverbial extra mile to show that these agents are actually viruses rather than some sort of unusual bacteria," says Eugene Koonin, a computational evolutionary biologist at the National Center for Biotechnology Information in Bethesda, Maryland.

But unlike other viruses, the pandoraviruses lack the gene for the capsid protein that typically forms a capsule around a

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virus's genes and are missing some key genes found in all other giant viruses and their relatives, including ones for replication. "They seem to be a new family unto themselves," Ghedin says.

Indeed, most of the pandoravirus genes don't look like any in known databases. "The lack of similarity might be an indication that they originated from a totally different primitive cellular lineage than bacteria, archaea, and eukarya," Claverie says. Add in other giant viruses, he says, and "these viruses might indicate that not only a fourth domain existed but also a fifth, a sixth, etc." Raoult goes so far as to suggest lumping all complex microbes—the various giant viruses plus archaea, bacteria, and microbial eukaryotes—into a new grouping he would call TRUC, an acronym for Things Resisting Uncomplete Classification—and the French word for stuff.

A class of their own. Pandoraviruses have a much bigger genome, an atypical shape, and different genes from megaviruses (*inset*), the next largest viruses known to date.

It's too soon to redraw the tree of life, several researchers caution. But some revision is already warranted, Suttle argues. "What the discovery of pandoraviruses and mimiviruses makes increasingly clear is that the 'domains' of life is an archaic concept that does nothing other than keep viruses from their rightful place at the table where the story of the evolution of life is told."

–ELIZABETH PENNISI