

Ever-Bigger Viruses Shake Tree of Life

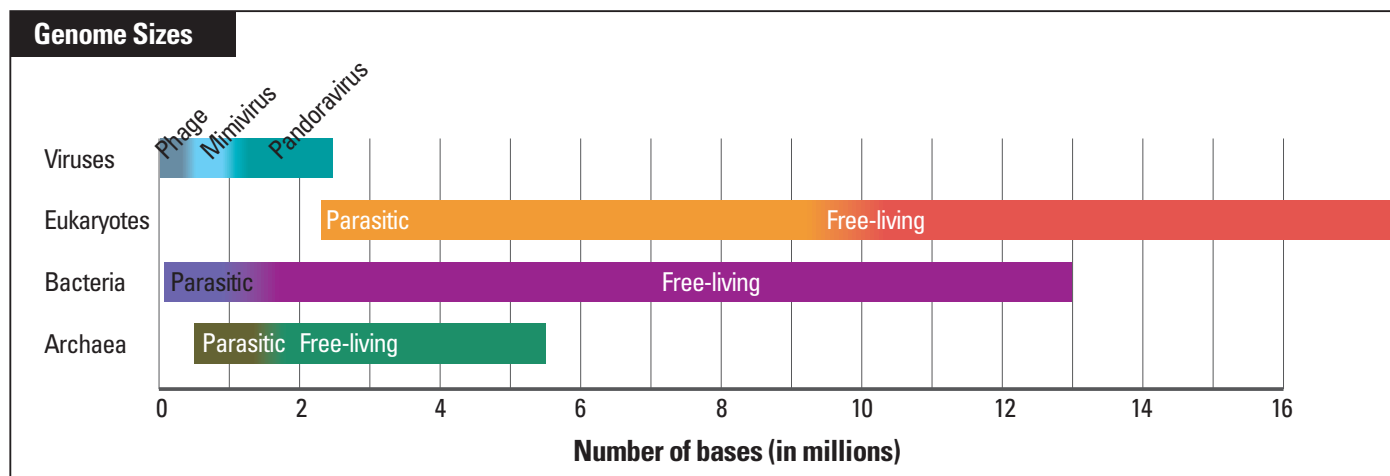
“It’s like finding a sasquatch,” says Elodie Ghedin, a virologist at the University of Pittsburgh in Pennsylvania. That’s one of the amazed reactions to the discovery, reported on page 281, of two new viruses with by far the largest genomes ever seen in a virus, including one that’s bigger than the genomes 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.

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 non-

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



“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

viruses 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

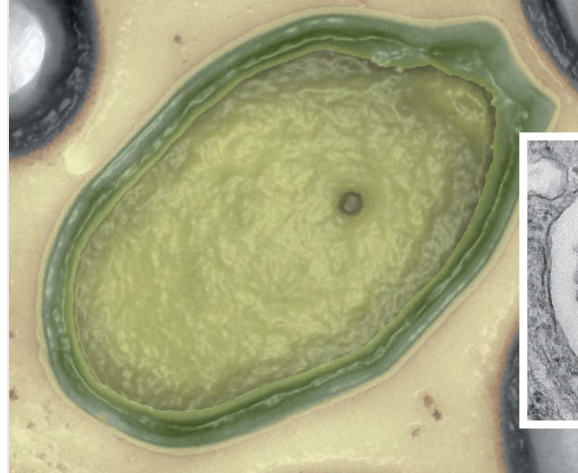
two of them were found almost simultaneously from very distant locations either indicates we were incredibly lucky or that they are not rare,” Claverie says. “They are probably everywhere.”

Because of their size, the pandoraviruses appeared bacterial-like 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.

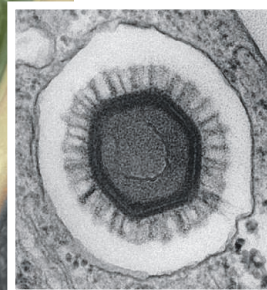
But unlike other viruses, the pandoraviruses lack the gene for the capsid protein that typically forms a capsule around a

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



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.



plus archaea, bacteria, and microbial eukaryotes—into a new grouping he would call TRUC, an acronym for Things Resist-

ing Uncomplete Classification—and the French word for stuff.

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

FUNDING

Germany Debates How to Strengthen Universities

BERLIN—Germany's recent push to boost a handful of its universities to the world's top ranks got a yellow light this week. A prominent advisory council recommended taking a break from the national competition to find, and fund, Germany's top schools. Funding should focus on strengthening a broad base of research—and teaching—at the country's universities, according to a 15 July report from the German Council of Science and Humanities (*Wissenschaftsrat*).

A relatively robust economy has allowed the government to increase funding for the country's major nonuniversity research organizations by 5% per year since 2011. But many university-based scientists see little of the money because the constitution prohibits the federal government from funding universities directly. A pair of agreements between the federal and state governments did pump billions of euros into universities through a "Higher Education Pact" that funds the growing number of students and an "Excellence Initiative" to support university research and encourage a few schools to strive for the world's top ranks. But not all universities have thrived.

In Germany, education is controlled by the *Länder* (states). Many state budgets have not been generous to research so university-based researchers have become increasingly dependent on grant-based funding, particularly from the German Research Foundation (DFG). "The basic funding for the universities is eroding," says DFG President Peter Strohschneider.

Change is coming because the budget-boosting agreements end between 2015 and 2019, and national elections in September will decide who gets to set the policies that will take their place. Funding bodies and organizations of research institutes have in recent months offered varying views of how the system should be changed. But they all share one thing: "We all agree that the funding for universities has to be increased," says Peter Gruss, president of the Max Planck Society, which funds institutes independent of universities.

On 9 July, the Max Planck Society proposed establishing a system of Max Planck Professors and Max Planck Centers at universities neighboring its institutes. The Helmholtz Association, which runs Germany's large research centers such as the DESY accelerator in Hamburg and the German Cancer

Research Center in Heidelberg, floated a controversial idea late last year for starting its own granting program that would fund cooperative projects with universities.

This week's report from the *Wissenschaftsrat*, which includes scientists and politicians, was the most eagerly awaited. An earlier, rejected draft reportedly said that Germany should strive for up to five world-class universities. The final version, in contrast, takes a more egalitarian approach, saying that universities are the core of the research system. It proposes two new funding mechanisms to support top research at a broad spectrum of schools: establishing Merian professorships, named for 17th century naturalist and illustrator Maria Sibylla Merian, which would provide €1 million per year to each of 250 leading academics; and setting up roughly 40 Liebig Centers (named for chemist Justus von Liebig), to boost key research areas. The competition for top schools could be revisited in 10 to 15 years, the report says.

Council Chair Wolfgang Marquardt says that the recommendations are affordable if Germany takes seriously the goal of spending 3.5% of gross domestic product on research and development. But others are more cautious. "There's still a huge gap between these proposals and the realities faced by politicians," says Wilhelm Krull, secretary general of the Volkswagen Foundation, a private research funder. —GRETCHEN VOGEL



Under pressure. German universities haven't all benefited from government funding largess.