



NATIONAL PRESS RELEASE | PARIS | MARCH 3, 2014

30,000 year-old giant virus found in Siberia

A new type of giant virus called "*Pithovirus*" has been discovered in the frozen ground of extreme north-eastern Siberia by researchers from the Information Génomique et Structurale laboratory (CNRS/AMU), in association with teams from the Biologie à Grande Echelle laboratory (CEA/INSERM/Université Joseph Fourier), Génoscope (CEA/CNRS) and the Russian Academy of Sciences. Buried underground, this giant virus, which is harmless to humans and animals, has survived being frozen for more than 30,000 years. Although its size and amphora shape are reminiscent of *Pandoravirus*, analysis of its genome and replication mechanism proves that *Pithovirus* is very different. This work brings to three the number of distinct families of giant viruses. It is published on the website of the journal *PNAS* in the week of March 3, 2014.

In the families Megaviridae (represented in particular by *Mimivirus*, discovered in 2003) and Pandoraviridae¹, researchers thought they had classified the diversity of giant viruses (the only viruses visible under optical microscopy, since their diameter exceeds 0.5 microns). These viruses, which infect amoeba such as *Acanthamoeba*, contain a very large number of genes compared to common viruses (like influenza or AIDS, which only contain about ten genes). Their genome is about the same size or even larger than that of many bacteria.

By studying a sample from the frozen ground of extreme north-eastern Siberia, in the Chukotka autonomous region, researchers were surprised to discover a new giant virus more than 30,000 years old (contemporaneous with the extinction of Neanderthal man), which they have named "*Pithovirus sibericum*". Because of its amphora shape, similar to *Pandoravirus*, the scientists initially thought that this was a new member — albeit certainly ancient — of this family. Yet genome analysis on *Pithovirus* showed that this is not the case: there is no genetic relationship between *Pithovirus* and *Pandoravirus*. Though it is large for a virus, the *Pithovirus* genome contains much fewer genes (about 500) than the *Pandoravirus* genome (up to 2,500). Researchers also analyzed the protein composition (proteome) of the *Pithovirus* particle (1.5 microns long and 0.5 microns wide) and found that out of the hundreds of proteins that make it up, only one or two are common to the *Pandoravirus* particle.

Another primordial difference between the two viruses is how they replicate inside amoeba cells. While *Pandoravirus* requires the participation of many functions in the amoeba cell nucleus to replicate, the *Pithovirus* multiplication process mostly occurs in the cytoplasm (outside the nucleus) of the infected cell, in a similar fashion to the behavior of large DNA viruses, such as those of the Megaviridae family. Paradoxically, in spite of having a smaller genome than *Pandoravirus*, *Pithovirus* seems to be less reliant

¹ See the July 18, 2013 press release on the discovery of Pandoravirus: <http://www2.cnrs.fr/presse/communique/3173.htm>



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on the amoeba's cellular machinery to propagate. The degree of autonomy from the host cell of giant viruses does not therefore appear to correlate with the size of their genome — itself not related to the size of the particle that transports them.

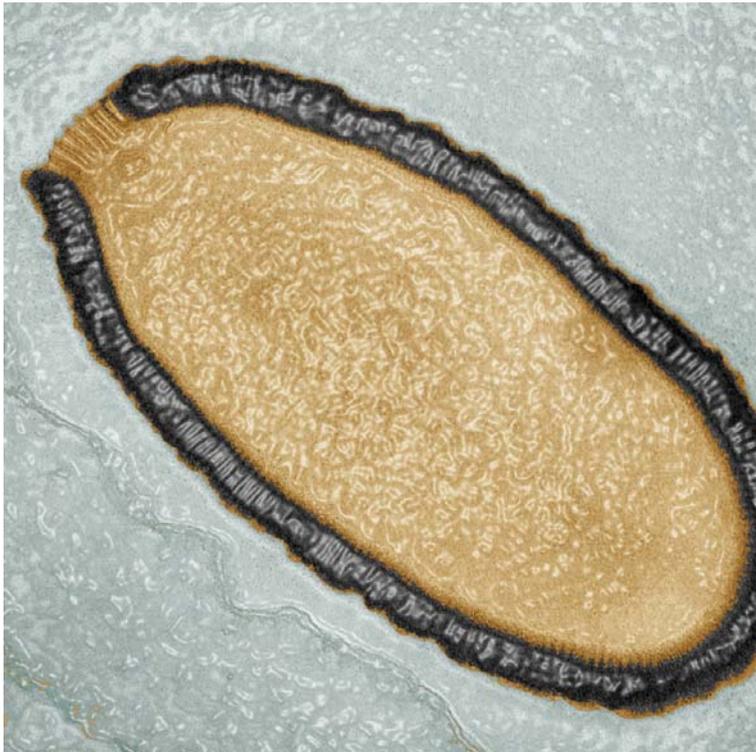
In-depth analysis of *Pithovirus* showed that it has almost nothing in common with the giant viruses that have previously been characterized. This makes it the first member of a new virus family, bringing to three the number of distinct families of giant viruses known to date. This discovery, coming soon after that of *Pandoravirus*, suggests that amphora-shaped viruses are perhaps as diverse as icosahedral viruses², which are among the most widespread today. This shows how incomplete our understanding of microscopic biodiversity is when it comes to exploring new environments.

Finally, this study demonstrates that viruses can survive in permafrost (the permanently frozen layer of soil found in the Arctic regions) almost over geological time periods, i.e. for more than 30,000 years (corresponding to the Late Pleistocene). These findings have important implications in terms of public health risks related to the exploitation of mining and energy resources in circumpolar regions, which may arise as a result of global warming. The re-emergence of viruses considered to be eradicated, such as smallpox, whose replication process is similar to *Pithovirus*, is no longer the domain of science fiction. The probability of this type of scenario needs to be estimated realistically. With the support of the France-Génomique infrastructure, set up as part of the national Investments for the Future program, the "Information Génomique et Structurale" laboratory is already working on the issue via a metagenomic study of the permafrost.

² These have a 20-sided polyhedral shape.



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Transmission electron microscopy color image of a *Pithovirus sibericum* cross-section. This virion, dating back more than 30,000 years, is 1.5 μm long and 0.5 μm wide, which makes it the largest virus ever discovered.

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Bibliography

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