

# Giant Viruses

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## Abstract

The discovery of what are referred to as Giant Viruses within the last few decades has become something of a phenomenon in biological circles. These viruses are found largely in the environment and are much larger in size and genomic complexity as compared to other viruses, rivaling bacteria in terms of composition. They are associated with amoebae and use amoebae as “factories” for replication. While they have not been directly linked to human disease, they have been isolated from human bodily fluids.

## Introduction

The isolation of a group of viruses known collectively as giant viruses of amoebae is relatively recent, and there is evidence of their existence going back at least 30,000 years [1,2]. There are several major groups of giant viruses that have been identified at this time. All are associated with amoebae. Among these are the groups Pithovirus, Mimivirus, Marisellevirus and Pandoravirus groups.

Giant viruses are extreme for many reasons [1,2]. First is their physical size which prevent them from passing through porcelain filters. Second is the size of their genomes which vary from 1.2 Mb for the mimivirus group to 2.5 Mb for the pandoravirus group [3]. Third, they are usually associated with amoebae. They use the amoebae for replication. In general, giant viruses reproduce in cytoplasmic compartments or “factories” which may be as large in size as a nucleus. This is one of the ways in which all giant virus are similar, the replication cycle [4]. All have a phagocytic entry mechanism to a host cell, and all have DNA release and replication in these factories. They all possess double stranded DNA. However, the replication cycle varies somewhat relative to the time of replication, and in some respects the degree of organization.

Pithovirus was first described in 2014. As mentioned above it was first seen associated with an amoeba dating back 30,000 years [1,2]. It has an oval wall and is open at one end, with a complex honeycomb type internal structure. Pithovirus contains in excess of 450 genes. Pithovirus has a circular genome and like all giants is ds DNA. It has about 600,000 base pairs, which translate 460 different proteins [3]. This much DNA encodes all the proteins needed to produce mRNA. Pithovirus undergoes its entire replication cycle in the cytoplasm of the host cell, not in the nucleus which makes it different from other “small” virus. The replication cycle may last as long as 20 hours, and is similar to pandoravirus. Pithovirus sibericum was found associated with amoebae in the soil dating back to the late Stone Age [2]. It was unearthed during an uncharacteristic thaw in the region. This virus group is comparable in genomic size to some bacteria.

Giant Virus was first isolated in hospital associated with Acanthamoeba polyphaga (mimivirus) [3]. It was isolated in a patient which presented to hospital with a respiratory infection. Since that time the search for the giant virus has become of primarily importance to environmental microbiologists. Mimivirus was first discovered and

identified as a giant virus in 2003 in France [4]. However, this agent was linked subsequently to a pneumonia outbreak in Leeds (UK) in 1992, for which a causative agent was not found at the time. Further examination revealed this as a giant virus which had infected an amoeba [5,6]. This indicates that the virus has been active and yet not detected for at least some decades in this case. They have a capsid of 500 nm and 75 nm long fibrils. These fibrils allow for attachment via glycans onto different types of fungi and bacteria. The genes of Mimivirus were found to encode proteins responsible for DNA repair and protein folding and metabolism of polysaccharides and lipids [7].

As with other giant viruses Pandoravirus are not at this time known to infect humans [8]. In comparison to Pithovirus, the Pandoravirus has 5 times as many protein coding sequences. They are found in the environment have been associated with contact lens solutions via their amoebae hosts. They are found in marine environments and sediment. The replication cycle for this group starts with viral penetration through phagocytic vacuoles. Pandoravirus reorganizes the host nucleus as a precursor for replication, with new particles being released about 10 hours after infection.

Marisellevirus was isolated in 2009 from a cooling tower France [9]. It is comprised of a 250 nm capsid and is icosahedral in shape. As with the other giant viruses this group is primarily isolated from the environment associated with an amoebae host. However, one member of this group the Senegalvirus was isolated directly from human feces from a healthy subject in Senegal.

## Infections in Humans

Giant viruses unlike other human and animal viruses have shown no clear direct link directly to human infections. What seems to be necessary is a host vector such as an amoebae for replication. But there is no “downstream” infection. There is always the presence of the protist. Many of these infections are respiratory in nature. There

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are also reports of infections due to contamination of contact lens cases for storage of lenses and solutions, and intestinal infections. In the case of the contact lens contamination there was also isolation of *Acanthamoeba*. However, the data indicate that once infected there is evidence of an immune response to the virus involved. Often the giant virus group is the Mimivirus. It is possible that the cause of overt symptoms such as respiratory distress or other types of inflammation are due to the presence of the amoebae, as well as the virus. This possibility is somewhat frightening as amoebae are difficult to treat. At this time there are no vaccine therapy against any giant virus to say nothing of the amoeba which frequently act as hosts [10].

## Conclusions

The recent discovery of giant viruses and their linkage to human disease represents an exciting possibility for a greater understanding of our world. They seem to be ubiquitous. They are found everywhere from forest, to the open oceans and more recently to humans. There is much that is not known. Can they cause disease on their own, or must they always be associated with amoebae? How expansive are they in nature and can they offer new opportunities for gene transfer and disease treatment because their genomes tend to be more complex than the “average” virus?

Frozen organisms like the giant viruses discussed above from the past may or may not in this instant case be a threat to humans in the present day. Science has no idea at this point what other ancient species of microbe exist that have yet to be unearthed due to climate change. What is certain is that these newly discovered organisms must be studied, and with the greatest of care.

Another issue that may be associated with giant virus is their potential use as a biological weapon. Since the cells and the genomes contained therein are large, like the pox virus, there may be

opportunities for placement of human harmful genetic code inside these viruses themselves. There are of course several problems associated with this, not least of which is the large-scale manufacture of these viruses, their storage until use and stability upon genetic manipulation. But there is the possibility that if weaponized these organisms could represent a tremendous threat to human health.

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