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Characteristics of Giant Viruses: Achantamoeba polyphaga Mimivirus, Pandoravirus and Tupanvirus: A Review of the Literature

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Abstract

'Giant viruses' are viruses that have a genome of >200,000 bp and have been shown to infect eukaryotic organisms such as algae and protists. Giant viruses viruses have unique characteristics in addition to being very large in size, these viruses have a complex genome structure so that they are able to reproduce independently in the host cell. independently in the host cell. Some of these viruses are Achantamoeba polyphaga Mimivirus, Pandoravirus and Tupanvirus. This review aims to summarize the research that has been done on the giant viruses that have been have been discovered. Methods used in writing this article were analyzed through searches on scientific databases such as PubMed, ScienceDirect and Google Scholar.
***Keywords**: Giant Virus; Mimivirus; Pandoravirus; Tupanvirus.*

Abstrak

‘Virus raksasa’ merupakan virus yang memiliki genom >200.000 bp dan terbukti dapat menginfeksi organisme-organisme eukaryotik seperti alga dan protista. Virus raksasa memiliki karakteristik unik selain berukuran sangat besar, virus-virus ini memiliki struktur genom yang kompleks sehingga mampu berkembang biak secara mandiri di dalam sel inang. Beberapa virus tersebut yaitu Achantamoeba polyphaga Mimivirus, Pandoravirus dan Tupanvirus. Tinjauan ini bertujuan untuk meringkas penelitian-penelitian yang sudah dilakukan mengenai virus-virus raksasa yang sudah ditemukan. Metode yang digunakan dalam penulisan artikel ini dianalisis melalui pencarian data pada basis data ilmiah seperti PubMed, ScienceDirect dan google scholar.
Kata Kunci: Virus Raksasa; Mimivirus; Pandoravirus; Tupanvirus.

INTRODUCTION

Since it was first discovered, viruses have been an interesting object of scientific research to be researched. Virus is a term used to describe an infectious agent that survives by multiplying itself in the host cell. Viruses are generally much smaller than bacteria so they are invisible to light microscopes and are able to pass through sterilization filters. In addition to being small, viruses also generally have very few genomes, making them highly dependent on host cells to be able to replicate [1].

Viruses were first visualized using electron microscopes and are still a hot debate among researchers to classify the link between viruses and living cells [2]. This is because viruses have unique and mysterious characteristics that make them biased between calling them living beings or not. Cells in general have genetic material in the form of DNA and RNA, but viruses, although they have a genome of genetic material, only consist of one of them either RNA or DNA. Its genome does not allow the virus to divide, produce ATP, and code for protein translations independently, making it necessary to use components in the host cell to do so [1].

The study of the unique features of viruses has been a source of discovery that has helped build the foundations of molecular biology and led to in-depth evolutionary studies. In recent years, the discovery of new gigantic viruses has become a research that has increasingly raised questions about the evolution and relationship of these viruses to their hosts.

In 2003 a giant virus named *Achantamoeba polyphaga* Mimivirus was first discovered in pneumonia patients infecting amoeba [3]. This virus has a very large size, much larger than bacteria and even almost equal in size to eukaryotic organisms. This discovery paved the way for the discovery of other giant viruses and gave rise to new families such as Mimiviridae, Pandoraviridae, Mollivirus, and Pithovirus [2].

'Giant virus' is a term that refers to a virus that has a genome of >200,000 bp. These viruses have been shown to infect eukaryotic organisms such as algae and protists. Giant viruses have unique characteristics that are different from viruses in general. In addition to being very large, these viruses have a complex genomic structure that makes them capable of multiplying independently within host cells. The unique genetic traits it brings make many scientists interested in digging deeper into the information contained in it. Further research on giant viruses is believed to answer scientific questions that remain a mystery and open to broader discoveries [4]. Thus, this review aims to summarize the studies that have been carried out on the giant viruses that have been discovered.

RESEARCH METHODS

The method used for writing this article is a literature review related to new viruses. Articles analyzed are obtained through searches on scientific databases such as PubMed, ScienceDirect, Google Scholar. The search was conducted using the keywords "new virus", "giant virus", "mimivirus", "pandoravirus" and "tupanvirus". This research was selected based on strict inclusion criteria including topic relevance, methodological quality, and contribution to the field of study of article writing.

HASIL DAN PEMBAHASAN

Acanthamoeba polyphaga Mimivirus (APMV)

Mimiviruses are giant DNA viruses that infect amoeba. Overall mimiviruses are +700 nm in size and have a DNA genome of 1.2 Mb. Mimiviruses were first observed in 1992 in cases of nosocomial pneumonia while investigating amoebas and are considered bacteria due to their much larger size than viruses in general and even larger than some types of prokaryotes [5]. In 2003, the results of transmission electron microscopy combined with relevant genomic data, the organism was successfully identified as a virus and called *Acanthamoeba polyphaga* Mimivirus (APMV). This discovery was the origin of the identification of a new family of Mimiviridae [4].

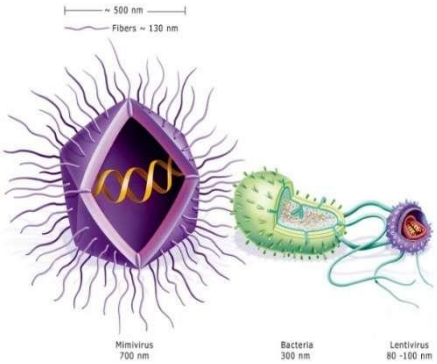

Figure 1. Mimivirus Size

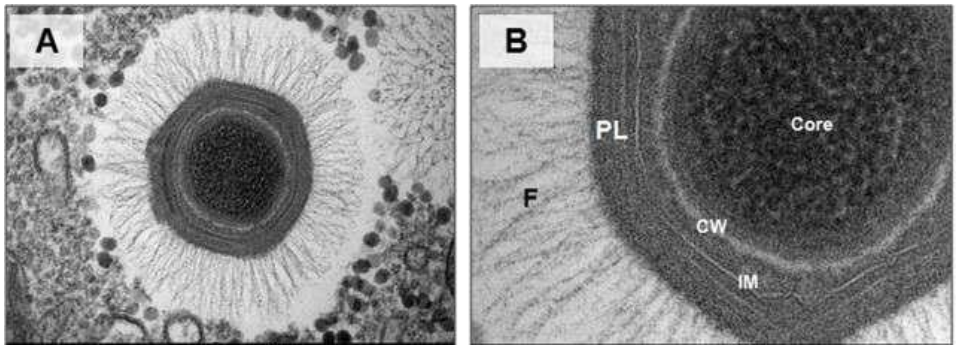

Figure 2. Structure of Mimiviruses

APMVs do not have an outer sheath, but they do have 120 nm long fibers associated with the capsid. These fibers are involved in the adsorption of viruses to the substrate. APMV encodes enzymes that synthesize polysaccharide complexes. Where these polysaccharides form a layer that functions where the fibers are embedded as a phagocytosis stimulus. The APMV has pseudo-iconoclastic symmetry, with a complex pentagonal surface region called a stargate. This stargate is the star where the viral genome is released during the viral replication cycle. Figure 2 shows the structure of the APMV. *The core* of the virus is the nucleus of the virus where the virus genome is. CW is the core membrane that protects the viral genome. IM is the outer membrane of the virus. PL is a polysaccharide layer that envelops the capsid and the fiber attachment site. F is the fibers that attach to the virus [6].

Mimiviruses have unique characteristics. It is able to exchange genetic material with its host and other parasites present in the same host cell. For example, Marseillevirus. APMV can exchange genomes with Marseilleviruses that also infect amoeba. Despite being a DNA virus that infects eukaryotic cells, mimiviruses never enter the host nucleus. It has the capacity to multiply in the cytoplasm of the host cell [7].

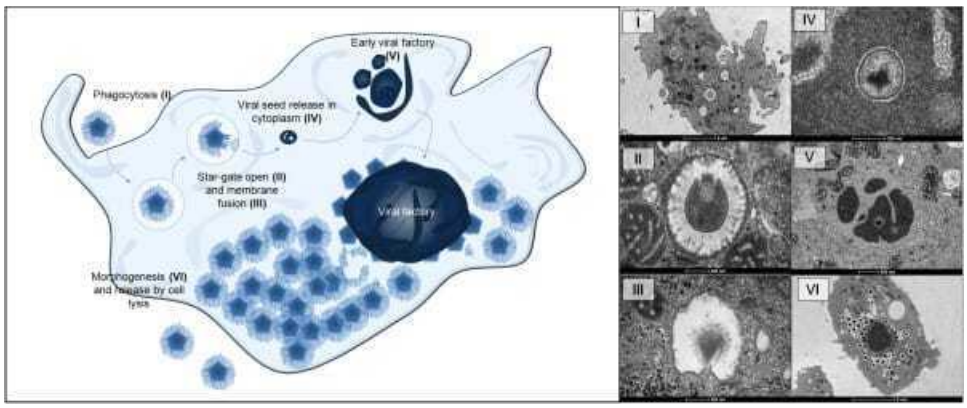

Figure 3. Mimivirus Replication

The APMV Replication Cycle starts from the phagocytosis process. The fibers of mimiviruses will attach to the cell membrane of the amoeba. The cell membrane will envelop the virus to form vesicles and insert them into the cell. The vesicles will fuse with the phagosomes and with the help of phagosome stragates in the viral capsid will open and release the virus seeds containing the genome into the cytoplasm. Viral replication

occurs in the cytoplasm. The manufacture of the factory of young viruses begins with the replication of the genetic material of the virus with the help of factors obtained from the host cell. After that, the genetic material will undergo transcription and translation, then the DNA will be packaged in the procapsid. Furthermore, the young virus will undergo morphogenesis with the development of other components such as cell membrane coating, pe; Polysaccharides and fibers are filtered to form an adult virus. After that, the host cell or amoeba will undergo lysis and the adult APMV will come out and look for a new host to stop by [7].

Mimiviruses have a MIMIVIRE system as a defense system against virophages that are often associated with the CRISPR-Cas System in bacteria to preserve their genomes. This is necessary because this virus can be infected by other viruses, namely virogate. Virophages that infect APMV will inject their genetic material. This genetic material will then be cut and the particles will be combined with the original genome of the mimivirus. After that, the gene particles of this virophage are displayed and will eventually be recognized by the cell so that if a similar virophage attacks, the defense system can directly attack it. This is also one of the barriers to whether the virus is a living thing or not. Because in general, viruses cannot be infected because they are not living creatures. However, this mimivirus can be infected by other viruses, so this is another consideration whether the virus is classified as a living thing or not [6].

The level of pathogenicity of APMV in humans is still being researched. This virus was detected in the lungs of patients with pneumonia. In addition, APMV can also grow in human peripheral blood mononuclear cells and induce immune reactions through the production of interferon type 1 (IFN). Nevertheless, so far APMV infection is not harmful to humans [5].

Tuvanvirus

Tupaviruses were first identified in 2018 with the discovery of two tupanvirus isolates found in soda lake samples, known as aquatic extreme environments and from marine sediments collected at a depth of 3000 meters. Tupanvirus is the first virus to be reported because it has a gene for amino-result tRNA synthetase for all 20 standard amino acids, which shows the class *of megaviricetes* of the *family mimiviridae.* The name tupanvirus was given in honor of the god of thunder (tupa) who was an important figure for the indigenous Guarani tribes in the United States [2].

Tupanvirus has a capsid that is ~450 nm in size which shows a *stargate structure* and is covered by fibrils, but unlike other viruses tupanvirus has a large cylindrical tail attached to the base of the capsid with a length of ~550 nm and a diameter of ~450 nm (including fibrils).

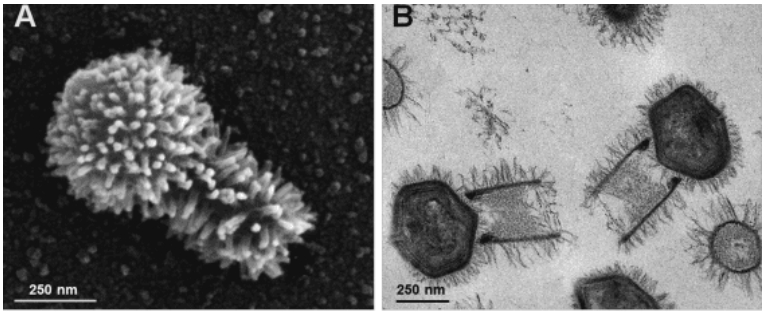

Figure 4. Morphological and replicative properties of tupanvirus (A). Transmission electron microscopy (TEM) of tupanvirus particles, showing mimivirus-like acapsids and cylindrical tails attached to their base (B).

The average size of tupanvirus virions is 1.2 ɥm which makes it possible to visualize using a microscope [8]. There is a lipid membrane inside the capsid which is similar to that of other giant viruses, which is linked by fusion with the phagosome membrane and the release of the contents of the capsid [9].

Tupanviruses contain genes that encode mannosa-specific lectins, also called mannosa-binding proteins, because they can induce the expression of cellular and viral mannose receptor genes that are well known to promote the attachment of amoebas to other cells. Tupanviruses are not pathogenic to humans but are better known as pathogens for protists because because tupanviruses are found amoeba, such as *acanthamoeba*, and also cannot replicate within human cells and so far research has not found any link between diseases caused by tupanviruses [8].

Tupanviruses replicate in such a way that viral particles can attach to the surface of the host cell and enter through phagocytosis, as the inner membrane part of the capsid fuses with the phagosomes of the host cell, the viral genome is released into the cytoplasm of the host cell. In the cytoplasm, the new part of the virus will be formed starting from the capsid to the tail, after the part of the virus is formed, the process of assembling a new virus will begin which will be released through cell lysis. Tupanviruses have the largest host range described so far among giant viruses that infect amoebas and can cause the termination of host rRNA which is likely related to host-nucleolus degradation [10].

Pandoravirus

Pandoravirus is a giant DNA virus that can infect amoeba of the genus *Acanthamoeba castellanii*. *Pandoravirus* has a genome that exceeds the genome of some eukaryotic microorganisms [11], with a very large proportion of non-homologous open reading frame (ORF) genes (ORFans) in any database. Approximately 70% of the predicted ORF pandoravirus gene [12]. *Pandoravirus* has quite unique morphological and genetic characteristics that have never been described before, namely like particles with an oval shape and the tip of the virus is ostiole, with a diameter of ~0.5μm and a length of ~1.0μm. In addition , *pandoravirus is characterized by the presence of a double-stranded DNA genome up to 2.5 Mb with a double-stranded linear composition, pandoravirus has a fairly large and neatly structured capsid that can protect several layers of proteins in it and is the largest genome in the virosphere, especially* Pandoravirus salinus *[13]*.

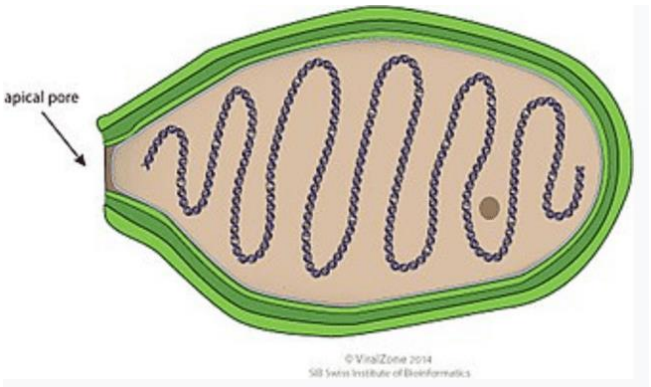

Figure 5. *Pandoravirus Structure*

(Antwerp M. H., 2015) pertama kali ditemukan oleh sekelompok ilmuwan yang sedang melakukan penelitian tentang virus raksasa yang menginfeksi amoeba pada tahun

2013, sampel yang diambil berasal dari sedimen sampel air laut serta air tawar yang kaya akan mikroorganisme. Dari hasil isolasi tersebut ditemukan dua spesies yang diidentifikasi yaitu *Pandoravirus salinus* dari sedimen air laut dan *Pandoravirus dulis* ditemukan pada sampel sedimen air tawar [13]. *Pandoravirus* ketiga yaitu *Pandoravirus inopinatum* yang ditemukan melalui analisis genom endosimbion dengan menggunakan sifat *Pandoravirus* . (Antwerpen M. H., 2015)Kemudian ditemukan kembali *Pandoravirus* jenis baru dengan menggunakan kultur sel *A. castellanii* yang diperoleh dari sampel air limbah serta sampel air danau soda yaitu virus *Pandoravirus pampulha* dan *Pandarovirus brasiliensis* [14].

Giant viruses are not pathogenic and do not cause disease to humans even though they are found lurking in the human body. According to some of the evidence found, pandoravirus has benefits for organisms present in the oceans to regulate several phytoplankton populations and contributes to the world's oxygen supply quite significantly. In addition, this pandoravirus is also expected to produce further biomedical and biotechnical innovations [15].

The process of pandoravirus replication occurs in the host cell, *A. Castellani,* by involving several processes, such as:

a) Phagocytosis: where virions will bind to the host cell and enter through the phagocytosis process by the host cell.
b) Fusion: the apical pores will open and then the virus sheath will fuse with the cell membrane, pandoravirus will release its genetic material into the host cytoplasm to enter the transcription and replication stages.
c) Assembly and lysis: new virions will be processed in the cytoplasmic factory, the nucleus will undergo *recycling* into viral membranes and new virions [1].

The following is an example of *the Pandoravirus* replication process in *A. Castellani cells*

Pandoravirus *replication* for all types of *Pandoravirus* species has the same cycle/stages [16]. Based on the image in section [B], it shows *that Pandoravirus* enters *Acanthamoeba castellanii* cells through the process of phagocytosis by the host cell. [C] amoeba protrudes the pseupod by involving the virus and inserts it into the vesicle structure (phagosome). [D and E] then phagosomes begin to fuse with other components whose structure resembles lysosomes and then release their combined contents to stimulate *the Pandoravirus* particles to peel off. [F] *Pandoravirus* has already begun to spread its genetic material to host cells.

CONCLUSION

The results of the study came to the conclusion that, since it was first discovered, the virus has been an interesting object of research to study. Viruses have a unique structure for survival. Over time, the discovery of giant viruses has opened up our perspective on viruses that are still very mysterious. Giant viruses are very large viruses with a genome of more than 200,000 bp. This virus is much larger in size than bacteria and has a different mechanism than viruses in general. Giant viruses do not rely too much on the host to be able to replicate. Some of the giant viruses that have been found include *Achantamoeba polyphaga* Mimivirus (APMV), Pandoravirus, and Tupanvirus. APMV was found to infect amoeba in pneumonia patients. Tupanviruses can cause cytotoxic effects on host cells. Pandoravirus is a giant virus with a genome that is much larger than any other giant virus and is the largest virus ever discovered to date. These viruses infect

eukaryotic organisms such as amoeba, but there are no further studies proving whether the virus can be pathogenic to humans.

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