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Review

The expanding family *Marseilleviridae*

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ABSTRACT

The family *Marseilleviridae* encompasses giant viruses that replicate in free-living *Acanthamoeba* amoebae. Since the discovery of the founding member Marseillevirus in 2007, 7 new marseilleviruses have been observed, including 3 from environmental freshwater, one from a dipteran, and two from symptom-free humans. Marseilleviruses have ≈250-nm-large icosahedral capsids and 346–386-kb-long mosaic genomes that encode 444–497 predicted proteins. They share a small set of core genes with Mimivirus and other large and giant DNA viruses that compose a monophyletic group, first described in 2001. Comparative genomics analyses indicate that the family *Marseilleviridae* currently includes three lineages and a pan-genome composed of ≈600 genes. Antibodies against marseilleviruses and viral DNA have been observed in a significant proportion of asymptomatic individuals and in the blood and lymph nodes of a child with adenitis; these observations suggest that these giant viruses may be blood borne and question if they may be pathogenic in humans.

Contents

Introduction

Giant viruses were first described in amoebae a decade ago, when *Acanthamoeaba polyphaga* mimivirus was identified in a cooling-tower water sample from England (La Scola et al., 2003; Raoult et al., 2007). This observation revolutionized the scientific perspective on viruses and their diversity and has generated considerable interest and debate in the field of evolutionary biology (Raoult et al., 2004; Moreira and López-García, 2009; Raoult and Forterre, 2008; Forterre, 2010; Boyer et al., 2010b; Raoult, 2013). Mimivirus was the largest known virus for a decade; this virus was isolated by co-culturing with *Acanthamoeba* spp., a culture strategy initially used to isolate legionella-like pathogens (Barker and Brown, 1994; Horn and Wagner, 2004; Raoult and Boyer, 2010; Rodriguez-Zaragoza, 1994). Mimivirus was the founder of a new viral family *Mimiviridae*; dozens of members of this

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family were subsequently isolated, mostly from water or soil and recently from pneumonia patients (Saadi et al., 2013b; La Scola et al., 2008; Fischer et al., 2010; Arslan et al., 2011; Yoosuf et al., 2012; Pagnier et al., 2013; Saadi et al., 2013a).

In 2007, a giant virus whose particle and genome sizes were approximately 2–3 times smaller than Mimivirus was isolated by culturing on *Acanthamoeba castellanii* (Boyer et al., 2009). This virus was named Marseillevirus and founded a new viral family officially recognized by the International Committee on Taxonomy of Viruses (ICTV) in 2013 (http://www.ictvonline.org/taxonomyHistory.asp?taxnode_id=20133581&taxa_name=Marseilleviridae) (Colson et al., 2013d). Over the past five years, the family *Marseilleviridae* has expanded, although it contains less members than the family *Mimiviridae* (Thomas et al., 2011; La Scola et al., 2010; Pagnier et al., 2013; Aherfi et al., 2013; Boughalmi et al., 2013b, 2013a; Popgeorgiev et al., 2013a; Lagier et al., 2012; Yutin et al., 2013). Four close relatives of Marseillevirus were isolated from water samples in France and Tunisia, one was isolated from a dipteran, and two were isolated from human stools and blood. These giant viruses have similar features compared to mimiviruses but differ in the size and morphology of the virions, their gene repertoire and replicative cycle. Recently, three new giant viruses of amoeba were described, including *Pandoravirus salinus* and *Pandoravirus dulcis* (Philippe et al., 2013), which became the largest known viruses, and *Pithovirus sibericum* (Legendre et al., 2014), which is related to marseilleviruses. Here, we review the discovery and features of marseilleviruses, including their similarities and differences with other amoebal giant viruses.

Discovery and morphological features of marseilleviruses

Marseillevirus was isolated in 2007 from the water of a cooling tower in Paris by co-culturing on *A. polyphaga* (Boyer et al., 2009) (Table 1; Fig. 1). Marseillevirus has a capsid of approximately 250 nm in diameter (Table 2). Cryo-electron microscopy revealed an ≈10-nm-thick capsid shell with a roughly icosahedral shape, surrounded by 12-nm-long fibers with globular ends. The nucleocapsid is present ≈5 nm below the capsid shell, potentially enclosed by a membrane. Lausannevirus, the second known member of the family *Marseilleviridae*, was described in 2011 by analysis of *A. castellanii* co-culture of a water sample collected in 2005 in the Seine river near Paris, at the inlet of a drinking water plant (Table 1; Fig. 1) (Thomas et al., 2011). Lausannevirus particles were initially observed as Gimenez-positive cocci; these viruses have an icosahedral shape, a diameter of 190–220 nm and are devoid of fibrils or tails. The Cannes8 virus was isolated from water in a cooling tower in Cannes, southeastern France (Aherfi et al., 2013). Tunisvirus and Fontaine Saint-Charles virus were isolated from freshwater collected in decorative fountains in Ariana, a suburb of Tunis, Tunisia, and Marseille, France, respectively (Aherfi et al., 2014; Pagnier et al., 2013). The morphological characteristics of these viruses were similar to those of previously described marseilleviruses.

The Insectomime virus was isolated from the internal organs and digestive tract of a larva of a dipteran, *Eristalis tenax*, a pollinator commonly known as the drone fly (Table 1; Fig. 1) (Boughalmi et al., 2013a). This larva was one of 86 larvae collected from two reservoirs of stagnant water in the center of Tunis, Tunisia. The larval surface was decontaminated with 96% ethanol and then washed with sterile Page's amoebal saline buffer. The Insectomime virus was isolated using a high-throughput culture procedure with monolayers of *A. polyphaga* in 12-well microplates (Boughalmi et al., 2013a). The internal organs and digestive tract were harvested under sterile conditions from the larva and wrapped in paraffin; these samples were positive for viral culture, whereas culture and PCR testing of the larval surface and washing solution were negative (Boughalmi et al., 2013a). The Insectomime virus was the first amoebal giant virus isolated from an insect. Its morphology and the diameter of the viral particle (225 nm) suggested that it was a Marseillevirus, which was further confirmed by genomic analysis. Insect larvae and *Acanthamoeba* spp. share the ecological niche of stagnant water, and the Insectomime virus may have entered the insect larva by direct ingestion or through ingestion of an infected amoeba. Both amoebae and viruses were previously described in insects (Otta et al., 2012; Muli et al., 2014; Evans and Schwarz, 2011; Li et al., 2014).

Senegalvirus was serendipitously discovered during metagenomic analysis of the bacterial diversity in the human gut microbiota from a lean, healthy African individual (Table 1; Fig. 1) (Lagier et al., 2012). This study included ultra-deep

Table 1
Source of marseilleviruses and their main genomic features.

Reference	Virus name	Source	Country	Collection year	Description year	Genome sequencing technology		Genome size (kilobase pairs)	G+C content (%)	GenBank accession no.	Number of genes
						454 Roche	SOLiD				
(Boyer et al., 2009)	Marseillevirus	Water, cooling tower	France (Paris)	2007	2009	+		368	45	GU071086	457
(Thomas et al., 2011)	Lausannevirus	River water (Seine)	France	2005	2011	+		346	43	NC 015326	444
(Aherfi et al., 2013)	Cannes8 virus	Water, cooling tower	France (Cannes)	2008	2013	+	+	374	45	KF261120	483
(La Scola et al., 2010)	Fontaine Saint-Charles virus	Water, fountain	France (Marseille)	2008	–	+	+	–	45	–	473
(Boughalmi et al., 2013b; Aherfi et al., 2014)	Tunisvirus	Water, fountain	Tunisia (Ariana)	2012	2014	+		382	43	KF483846	484
(Boughalmi et al., 2013a)	Insectomime virus	Insect	Tunisia	2012	2013	+		386	43	KF527888.1	477
(Lagier et al., 2012b; Coleson et al., 2013b)	Senegalvirus	Stool	Senegal (N'Diop)	2012	2012	+		372	45	JF909596-JF909601	497
(Popgeorgiev et al., 2013b)	Giant blood Marseillevirus	Human blood	France (Marseille)	2013	2013		+	357	–	–	–