LINK TO ORIGINAL ARTICLE
LINK TO INITIAL CORRESPONDENCE

What makes a virus a virus: reply from Raoult and Forterre

Didier Raoult and Patrick Forterre

The correspondence on our Opinion article (Redefining viruses: lessons from mimivirus. *Nature Rev. Microbiol.* **6**, 315–319 (2008)[1]) by Wolkowicz and Schaechter (What makes a virus a virus? *Nature Rev. Microbiol.* 16 July 2008 (doi:10.1038/nrmicro1858-c1)[2]) has allowed us to clarify some of the elements of our virus definition[1]. The authors rightly insist that the phenomenon of disappearance and reappearance of a virus (eclipse phase) is a major characteristic of viruses. They then go a step further, however, to suggest that it is the most fundamental aspect of a virus and propose to use this feature, instead of the capsid, to define viruses. Although the eclipse phase is informative in terms of virus description and could be added to our virus definition, we think that such a feature cannot be solely used to define viruses, because it is a phenotypic trait that cannot readily be assigned to a particular gene or set of genes (unlike the capsid) in the viral genome. Consequently, a definition of viruses that is based only on such properties would have a pre-Darwinian flavour (similar to the prokaryote or eukaryote classification system).

Phenotypic classification systems can easily be rendered obsolete by further discovery or lead to endless discussions about the definition of the phenotypic properties themselves. For example, the prokaryote and eukaryote classification system has been challenged by the discovery of bacteria (prokaryotes) that have a nucleus[3]. If viruses are defined as organisms with a cycle of disappearance and reappearance, it could be argued that most eukaryotes also have this feature. Indeed, if the human organism is assimilated as a functional integrated collection of organs, one might also consider that the organism has disappeared in the germinal cells and that the human cycle alternates between various forms, one that is a collection of organs and one that is a single-celled organism during reproduction. Similarly, the virus alternates between a cellular form of organization (the intracellular viral factory), a simple molecular form (the viral genome) and a complex molecular form (the virion). Remarkably, a cellular organism can be also reconstituted (at least in the laboratory) from a single molecule. A recent study showed that injection of an *in vitro* synthesized bacterial genome into a recipient cell led to the generation of bacteria with phenotypes that corresponded to the inoculated genome[4]. This experimental work clearly demonstrated that an isolated bacterial genome is sufficient to create a cellular organism. If this can be achieved in the laboratory, we cannot exclude the possibility that it could happen in nature. Therefore, in these experiments, bacterial and viral nucleic acids[5] are strictly comparable, making it necessary to classify them based on their coding capacity.

We think that the existence of genes which encode the capsid is the only positive genotypic trait that is currently useful for the definition of viruses. Using capsids, we can distinguish between viruses and selfish nucleic acids that lack capsids (for example, satellite viruses, satellite DNA or viruses). Focusing on the capsid also builds on the finding of Dennis Bamford and colleagues[6] that viral lineages should be primarily defined according to the evolutionary relationships of their capsids. We define viruses as capsid-encoding organisms and not capsid-harbouring organisms because the definition of capsid-encoding organisms is genotypic, whereas the definition of capsid-harbouring organisms is phenotypic and could be misleading (for example, arenaviruses harbour ribosomes from their hosts in their capsid). Furthermore, viruses encode the capsid during both their intracellular stage (viral factories) and when they are a single nucleic acid.

Wolkowicz and Schaechter[2] raise an interesting point: how can we distinguish the capsid from other capsid-like subcellular structures? This would require us to precisely define 'capsid', as capsid-encoding genes can be integrated into cellular genomes and can be used by the cell for new purposes. In our opinion, a capsid is the structure that is used to disseminate a genome that encodes the capsid proteins.

Didier Raoult is at the Unité des Rickettsies, IRD-CNRS UMR 6236, IFR-48, Faculté de Médecine, 27 Bd Jean Moulin, 13385 Marseille, France.

Patrick Forterre is at the Institut Pasteur, 25 rue du Docteur Roux, 75015 Paris1, France, and the University Paris Sud, Institut de Génétique et Microbiologie, CNRS, UMR 8626 IRF-115, Centre d'Orsay, 91405 Orsay, France.

Correspondence to D.R.
e-mail: didier.raoult@gmail.com

1. Raoult, D. & Forterre, P. Redefining viruses: lessons from Mimivirus. *Nature Rev. Microbiol.* **6**, 315–319 (2008).
2. Wolkowicz, R. & Schaechter, M. What makes a virus a virus? *Nature Rev. Microbiol.* 16 July 2008 (doi: 10.1038/nrmicro1858-c1).
3. Fuerst, J. A. Intracellular compartmentation in planctomycetes. *Annu. Rev. Microbiol.* **59**, 299–328 (2005).
4. Lartigue, C. *et al.* Genome transplantation in bacteria: changing one species to another. *Science* **317**, 632–638 (2007).
5. Smith, H. O., Hutchison, C. A., Pfannkoch, C. & Venter, J. C. Generating a synthetic genome by whole genome assembly: phiX174 bacteriophage from synthetic oligonucleotides. *Proc. Natl Acad. Sci. USA* **100**, 15440–15445 (2003).
6. Bamford, D. H., Grimes, J. M. & Stuart, D. I. What does structure tell us about virus evolution? *Curr. Opin. Struct. Biol.* **15**, 655–663 (2005).