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Sputnik and Mavirus: more than just satellite viruses

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In a recent Comment (Virophages or satellite viruses? *Nature Rev. Microbiol.* **9**, 762–763 (2011))[1], Krupovic and Cvirkaite-Krupovic discuss the classification of the virophages Sputnik and Mavirus — viral parasites of *Acanthamoeba polyphaga* mimivirus (APMV) and *Cafeteria roenbergensis* virus (CroV), respectively — and argue that they should be grouped among the satellite viruses. As the authors correctly point out, many of the features observed in Sputnik and Mavirus can also be found among classical satellite agents. However, the authors do not acknowledge two important points that could make all the difference.

First, Sputnik and Mavirus cannot be considered satellite viruses, as they are not "sub-viral agents", defined as entities that are smaller than viruses but with virus-like properties and "which lack genes that could encode functions needed for replication", as stated by the International Committee on Taxonomy of Viruses (ICTV)[2]. Instead, virophages appear to be fully functional viruses, as they encode their own proteins for particle structure and DNA replication. On the one hand, the capsid proteins of Sputnik, Mavirus and Organic Lake virophage (OLV) are related to each other[3–5] but bear no significant sequence similarity to their giant virus counterparts, even though they are likely to adopt the double-jelly-roll fold that is typical of capsid proteins from viruses of the bacteriophage PRD1–adenovirus lineage (which includes APMV and CroV)[6]. The DNA replication systems of virophages, on the other hand, differ from one species to the next; Mavirus encodes a predicted protein-primed B-family DNA polymerase[4], whereas a recently described phage T7-like DNA polymerase (fused to a helicase) is found in Sputnik and OLV[5,7]. It has been noted that virion structure tends to be highly conserved, whereas replication systems are interchangeable[8]. Virophages are no different in this regard. So, if Sputnik and Mavirus are not subviral, why are they dependent on co-infection by APMV and CroV?

The main novelty of Sputnik and Mavirus, and this is my second point, is that they are the first viruses to truly infect another virus inside a common host cell (FIG. 1). Giant viruses such as APMV and CroV replicate in large cytoplasmic virion factories, and encode an enzymatic complexity that is unrivalled among viruses and includes a presumably complete transcription apparatus, which is packaged in the virion and used to initiate viral gene transcription at the early stage of infection[9–12]. Although yet to be confirmed experimentally, Sputnik and Mavirus appear to depend on the transcription system of their associated giant viruses, as strongly suggested by the specific promoter and polyadenylation signals that are shared between these virophages and their giant viruses[4,13,14]. Consequently, if dependence on another organism's transcription system is sufficient for classification as a subviral agent, then we must consider all but the most complex DNA viruses as satellite viruses, as the majority of them depend on the transcription machinery of the host cell. Some people will object to granting viruses 'organism' status, but the idea of viewing the intracellular phase of a viral life cycle as a viral organism is neither new nor unreasonable (see, for example, Forterre's virocell concept[15]) and becomes especially evident in the case of giant viruses, the virion factories of which harbour a biochemistry that is complex enough to sustain infection by smaller viruses. Along these lines, I prefer to call APMV and CroV 'host' viruses rather than 'helper' viruses.

In conclusion, I agree with Krupovic and Cvirkaite-Krupovic when they argue that virophages do not represent a new biological entity. However, in the absence of experimental evidence suggesting otherwise, neither can we currently classify these parasites as subviral agents. Krupovic and Cvirkaite-Krupovic state that "Sputnik and Mavirus are likely to be members of the PRD1–adenovirus lineage that emerged from 'autonomous' viruses" (REF. 1). As discussed above, Sputnik and Mavirus still appear to be 'autonomous', bona fide viruses today, with the distinguishing feature that the organisms they infect are viral themselves. The taxonomic classification of Sputnik, Mavirus and other similar agents yet to be discovered should reflect this special lifestyle. Let us therefore not make these grown-up viruses sit at the kids' table by grouping them with the satellite viruses.

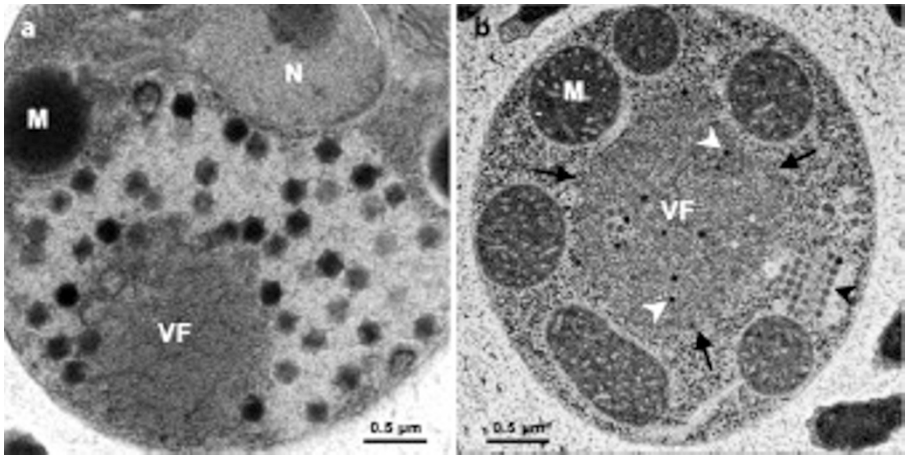

Figure 1 | **'Healthy' and 'sick' *Cafeteria roenbergensis* virus organisms. a** | Transmission electron micrograph of a Mavirus-free *Cafeteria roenbergensis* virus (CroV) virion factory (VF) producing CroV particles inside a *C. roenbergensis* cell. The cell nucleus (N) and a mitochondrion (M) are visible. **b** | The CroV factory shown here (outlined by arrows) is infected with Mavirus. No CroV particles are visible; instead, Mavirus particles are present inside the factory (white arrowheads) and in an adjacent crystalline array (black arrowhead). Image courtesy of C. A. Suttle, University of British Columbia, Canada.

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Competing interests statement
The author declares no competing financial interests.

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