A Need to Discover the World of Giant Viruses

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The world of giant viruses was brutally opened up at the beginning of the 21st century when a microorganism visible under the microscope, Gram stained, and which had been considered a bacterium for several years, was identified as the largest virus known at the time: it was Mimivirus [1, 2]. Its genome contained more than 1,200 genes and had the particularity, given the wealth of information it contained, to harbor genes common to bacteria, archaea and eukaryotes [3]. To me, this particular feature was the most striking, and I postulated immediately for the publication of the genome, believing that this virus might be representative of a fourth domain [3]. This caused various reactions, in spite of a subsequent classification into four branches using genes encoding for RNA polymerase showing four groups: giant viruses, archaea, bacteria and eukaryotes [4, 5]. For a while, I was the only one to believe in the existence of a fourth domain, which was challenged both by Jean-Michel Claverie and C.E. Woese [6]. We proposed later, based on these data, to create a new classification splitting organisms into capsid-encoding organisms and ribosome-encoding organisms [7]. In this issue, the specificity of codon and amino acid use of this group of viruses is reported [8].

Since then, we have reported the existence of a new family of viruses, *Marseilleviridae* [9], the first strain being *Marseillevirus* [10]. The recent discovery of a new giant virus, considered to be an intracellular eukaryotic parasite for 15 years [11], shows that the world of giant viruses keeps expanding and challenges the traditional classifica-

tion of microbes [2]. As a matter of fact, in the 20th century, some giant viruses were considered for a long time to be bacteria or parasites because the size factor biased their initial viral classification. Indeed, the established definition of a virus during the 20th century considered that all viruses should have at least one dimension of less than 0.2 μm [2, 7]. Giant viruses pose a problem to traditional virology techniques because purification techniques prior to virome study involve a filtration that removes giant viruses [12–14]. We were recently able to show that, when avoiding 0.2- μm filtration, giant viruses belonging to the *Marseillevirus* family could be found circulating in the blood of asymptomatic patients [13, 14]. In addition, for now, PCR techniques have unfortunately demonstrated little sensitivity because, due to the high variability of these viruses, tools were lacking to identify them [2, 15]. Culture techniques have indeed enabled the isolation of these viruses for the first time in human stool samples, with a reference reported in this paper [16]. New strategies for culture, purification [17] and isolation techniques [16] are reported in the present issue. Also, for the first time, these techniques have enabled the isolation of Mimivirus from a respiratory sample [18, 19] and the stools of a patient with pneumonia [20]. However, it is likely that serology is more effective in the detection of specific antibodies against the *Marseilleviridae* family, as related in Gilbert Greub's work in this journal [21].

These data confirm that both Mimiviridae and *Marseilleviridae* may be found in humans [19]. Mimivirus

seems to be linked to pneumonia and Marseillevirus is associated with asymptomatic carriage into blood [13] or in feces [22]. A case of adenitis in a young child has been identified [14] and antibodies to this virus have been found in blood donors [13, 21].

Finally, it is possible to find these viruses in many environmental samples, in sea and soil [16], and also in insects [23]. A large part of the viral world likely eluded us due to a definition problem related to the size of these viruses. In one paper of this issue, I propose abandoning the term domain (used to define living organisms based on the ribosome), which divided the microbial world into three after the prokaryote/eukaryote dichotomy in the 20th century and the definition of microbes as a sole entity in the 19th century [2]. My proposal, TRUC, which

offers a classification into four branches, is probably transitory and will most likely have to be modified over time as our knowledge of the microbial world increases.

In conclusion, this issue of *Intervirology* makes it possible to understand that the knowledge of viruses in the 21st century challenges our existing approach by integrating viruses such as microorganisms likely to be themselves infected by other viruses, virophages able to regulate their growth [24, 25] and, finally, viruses and virophages that can be infected themselves by selfish genes, polintons and transpovirons [25, 26] which act as gene vehicles from one organism to another. We are at the beginning of a great revolution in virology and this issue of *Intervirology* may contribute to the further discovery of giant viruses that are as yet an unknown.

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