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Virus infection

Hunting archaeal viruses

Viruses are obligate parasites that need host cells to replicate. They can infect members of all domains of life, as became clear soon after the first viruses were discovered in the 1890s. Ivanofsky and Beijerinck independently found that tobacco mosaic disease was caused by a 'filterable substance', also coined virus. Their work was followed by that of d'Herelle and Twort, who discovered that bacteria could also be attacked by a filtered substance, which was named 'bacteriophages'. Once electron microscopy became available, both filterable substances were shown to consist of viral particles.

With some exceptions, viruses isolated on animals and humans were mostly found to have an icosahedral or spherical shape, whereas those infecting bacteria showed a head-tailed morphology. By the second half of the twentieth century, the rate of discovery of viral morphotypes had slowed and viral diversity seemed to be confined to a quite limited number of morphologies.

This view changed drastically in the 1990s, when scientists led by Wolfram Zillig pioneered the discovery of viruses infecting archaea. In the 1970s, Archaea, which were until that point classified as Bacteria, were proposed to form a separate domain of life. This proposition was met with much criticism at the time. However, a small group of scientists, including Zillig, studied the molecular biology of extremophilic archaea and their results underscored this proposition. Zillig was keen on developing genetic tools to explore archaeal transcription, and to this purpose he was in search of archaeal mobile genetic elements. He organized two sampling trips to acidic hot springs in Iceland (~pH 1–4 and ~80 °C). In two papers published in 1993 and 1996, Zillig and colleagues reported their findings. They isolated a number of thermophilic archaea belonging to the Sulfolobales by establishing enrichment cultures that mimicked the original conditions from which the archaea were sampled. Zillig succeeded in detecting several mobile elements, among which were four plasmids, which laid the foundation for genetic systems of Sulfolobales species.

In addition, Zillig and colleagues isolated viruses from the environmental samples. They observed the cell-free fraction with electron microscopy to study viral morphology. Surprisingly, these viruses did not appear like any other virus seen before. They found rod-shaped, DNA-containing viruses with terminal fibres; flexible filamentous viruses; and they isolated Sulfolobales strains that were lysogens for spindle-shaped viruses. This overwhelming diversity in a single sampling trip induced others to step into this new and exciting field. In the following years, several groups continued the hunt for archaeal viruses. Almost every new viral isolate showed a novel shape, such as a bottle, droplet or spiral.

As the number of isolated archaeal viruses steadily grew, it became clear that the original diversity observed by Zillig was representative for viruses infecting archaea that belong to Thermoproteota. These show an incredible diversity of viral morphologies, many of which were never detected for bacterial and eukaryotic viruses. Archaeal viruses are still sparsely sampled compared with viruses infecting other domains of life. As even this fairly low number of viruses displays great diversity, could this be only the tip of the iceberg?

Over the past decade, the structures of numerous archaeal viruses were resolved in molecular detail using whole-cell cryo-electron tomography. These structures revealed that several archaeal viruses package their genomes very tightly as rare A-form DNA, which could help these particles stand the extreme conditions in which they thrive.

Cryo-electron tomography uncovered relationships between viruses that could not be detected on the sequence level. For example, archaeal viruses with different shapes (flexible filaments versus stiff rods) contain capsid proteins with similar folds. In addition, certain protein folds are used by viruses across the domains of life, such as the double jellyroll fold of certain icosahedral viruses. These new insights helped to classify archaeal viruses and establish their relationships with viruses from other domains of life. Another question is whether these uniquely shaped viruses also infect in unusual ways. Indeed, some mechanisms, such as the usage of pyramidal egress structures, are used only by archaeal viruses. However, further mechanisms used by archaeal viruses show similarities with other domains of life, such as viral egress via budding (similar to enveloped eukaryotic viruses) or anti-viral defence with CRISPR–Cas (similar to bacteria).

> "Extreme environments proved a treasure trove for virologists"

Extreme environments proved a treasure trove for virologists. The archaeal viruses isolated from here are instrumental to understanding the origin and evolution of all viruses. In addition, the detected similarities of archaeal viruses with both viruses from eukaryotes and bacteria enhances unification of the viral world and induces scientists to study virus–host interactions across the domains of life.

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Competing interests
The author declares no competing interests.

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