ARCHAEAL BIOLOGY

A trove of Asgard archaeal viruses

Three different studies identify Asgardarchaeota-linked virus genomes that share commonalities with both prokaryotic and eukaryotic viruses, yet they represent independent phylogenetic groups.

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Archaea share cellular characteristics with both bacteria and eukaryotes[1] and are thought to bridge the evolutionary divide between these branches of the tree of life. With the discovery of the Asgardarchaeota phylum, known as Asgard archaea, the phylogenetic relationship between archaea and eukaryotes became more tightly linked, and members of this group are currently proposed as the closest known progenitor of eukaryotes[2]. Asgard archaea could hold clues to the origin and evolution of life on Earth, but understanding of this enigmatic lineage is limited by the dearth of cultured representatives. In this issue of *Nature Microbiology*, three papers shine a light on Asgard ecology by identifying viruses that infect them.

These studies make use of the CRISPR–Cas antivirus defence system, using it as an archive of past infections to identify and analyse virus genomes linked with Asgard hosts in metagenomic-sequencing datasets.

Knowledge about the composition and evolutionary history of the virosphere remains patchy, and this is particularly true when it comes to the archaeal virome.

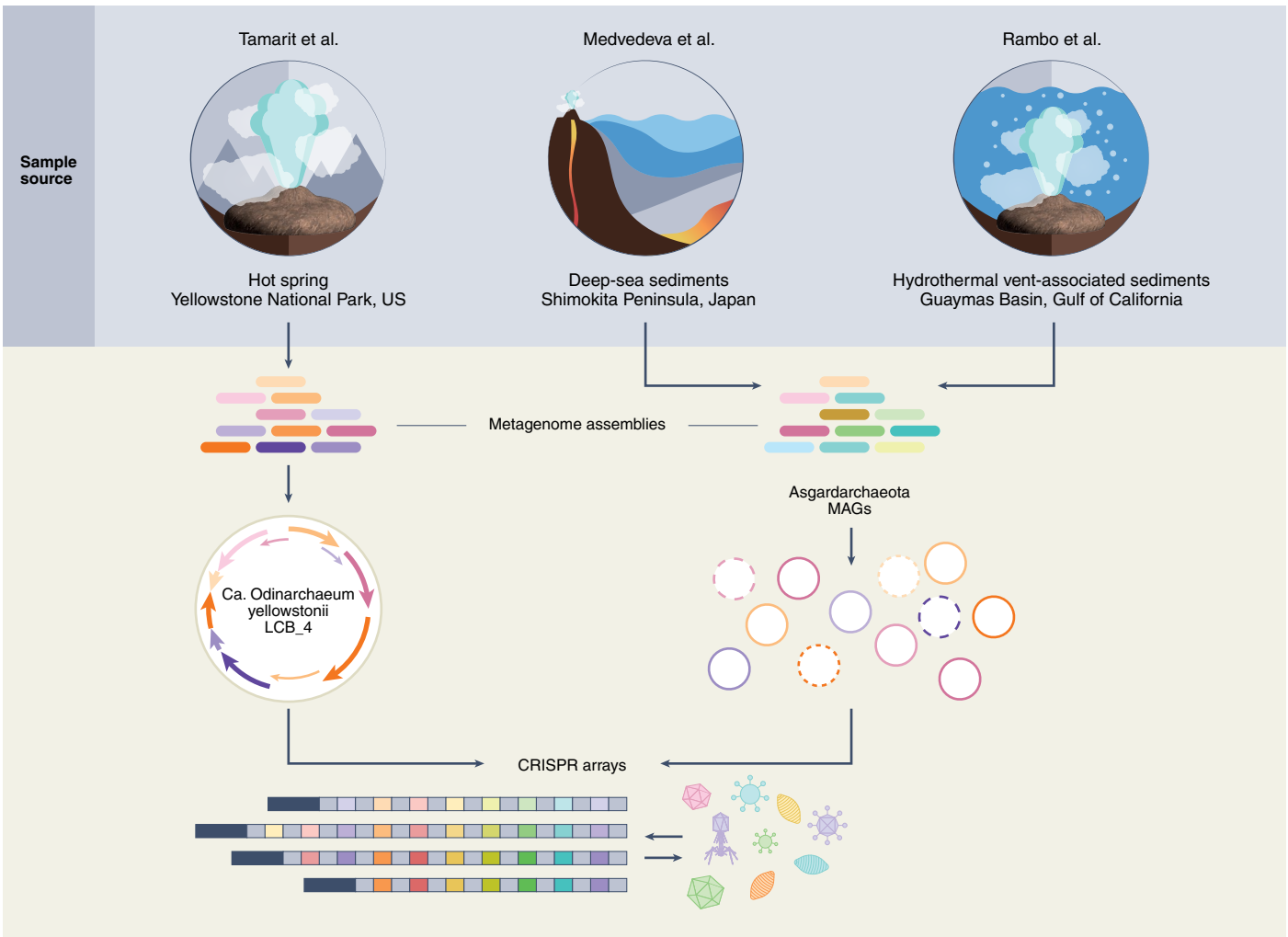

Fig. 1 | Identifying Asgard virus genomes using CRISPR arrays retrieved from Asgard MAGs. In three studies[7–9], metagenomic datasets were used to assemble Asgardarchaeota MAGs, and the CRISPR arrays within these genomes were subsequently used to match assembled viral contigs to their Asgard hosts.

Archaeal viruses characterized to date infect Halobacteriota, Methanobacteriota and Thermoproteota phyla, and most have been isolated from hypersaline or hot environments. Some of these archaeal viruses share homologous protein families with bacterial or eukaryotic viruses, which suggests that they have common evolutionary origins[3]. However, most archaeal virus families are uniquely associated with archaeal hosts and represent independent lineages[4].

Many overlaps in viral infection physiology hint at the evolutionary connections between eukaryotic and archaeal branches on the tree of life. Several host cellular processes that are required by a number of eukaryotic viruses to successfully infect cells, such as intracellular trafficking and vesicle formation and export, are thought to be executed by homologous groups of proteins in Asgard archaea and eukaryotes[5]. Additionally, the discovery of nucleus-like viral factories, generated by eukaryotic nucleocytoplasmic large DNA virus and bacteria-infecting jumbophages, has fueled the hypothesis that interactions with viruses may have played a role in nucleus emergence and eukaryotic evolution[6]. Are viruses that infect Asgard archaea related to eukaryotic viruses? Furthermore, what can we learn from them about the evolution of eukaryotic viruses?

By sampling deep-sea sediments known to be enriched in Asgard archaea, Medvedeva et al[7]. and Rambo et al[8]. generated multiple metagenomic-assembled genomes (MAGs) belonging to the Lokiarchaeaota, Thorarchaeota and Helarchaeota clades and retrieved multiple associated viruses through spacer sequences stored in the host CRISPR arrays (Fig. 1). CRISPR arrays are genomic archives of past infections and have the potential to establish links between uncultivated virus–host pairs. The major capsid proteins of the viruses identified exhibit the HK97-like fold, a structure typical of a large group of head-tailed viruses infecting archaea and bacteria (*Caudoviricetes*), but are also characteristic of the eukaryotic-infecting *Herpesvirales* clade.

Interestingly, while the *Caudoviricetes*-like genomes discovered by Medvedeva et al. exhibit genome sizes typical for archaeal head-tailed viruses, the viruses reported by Rambo et al. are substantially larger and exhibit genes predicted to be involved in genome replication and proofreading that have not yet been described in other archaeal viruses, but they have been found in eukaryotic giant viruses and in the genome of corynebacterium virus BFK20. Nevertheless, these genomes appear unrelated to jumbophages, and they do not show enhanced proportions of genes related to eukaryotic nucleocytoplasmic large DNA viruses, which are known to form nucleus-like viral factories. Thus, these viruses seem most closely related to prokaryotic *Caudoviricetes*, without significant eukaryotic features, and are unlikely to have played a role in nucleus emergence.

The study by Medvedeva et al. and a third study, by Tamarit et al.[9], which assembled a complete genome of *Candidatus* Odinarchaeum yellowstonii LCB_4 together with its CRISPR-targeted mobile genetic elements (Fig. 1), describe an additional virus group. The new virus genomes share little similarity with previously reported viruses but highlight connections between prokaryotic and eukaryotic viruses. The group, named Skuldviruses, is likely to represent tailless icosahedral viruses, which have a capsid morphology that is shared by bacterial, archaeal and eukaryotic viruses. On the basis of genome content and the structure of the major capsid protein, Skuldviruses are suggested to be members of a new virus order within the *Tectiliviricetes*. This class comprises two orders with bacterial hosts, one with an archaeal host and one with eukaryotic hosts. Skuldviruses do not seem to be closely related to the eukaryotic-infecting *Adenoviridae* within this class, but rather form a divergent group.

Overall, the findings of the three studies provide important new insight into the virosphere of one of the most enigmatic archaeal clades. While the host genomes appear to have a significant proportion of eukaryote-like features, the reported Asgard archaea viruses are not particularly closely related to eukaryotic viruses. Instead, the viruses are related to viruses infecting both archaea and bacteria and exhibit unique features that place them in a distinct position within the virosphere.

Nevertheless, this does not exclude the possibility that other viruses infecting Asgard archaea are at the archaea–eukaryote interface. Owing to the lack of cultured representatives, the current studies are limited to identifying virus contigs targeted by the CRISPR immune system. However, the CRISPR system is not effective against viruses that form nucleus-like structures or that can evade the CRISPR system. Different methods linking viruses and host, such as PhageFISH[10] or single-cell viral tagging[11], may help to identify other viruses infecting uncultivated members of the Asgard archaea. Finally, although these metagenomics studies are a critical first step in understanding this unexplored facet of Asgard archaea, in silico approaches cannot replace the information that could be gained from isolated virus–host systems. Successfully culturing representatives of Asgard hosts and the viruses that infect them will be the next frontier in understanding the importance of this enigmatic phylum. ❐

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References

1. Rivera, M. C. et al. *Proc. Natl Acad. Sci. USA* **95**, 6239–6244 (1998).
2. Spang, A. et al. *Nature* **521**, 173–179 (2015).
3. Koonin, E. V. et al. *Microbiol. Mol. Biol. Rev.* **84**, e00061–19 (2020).
4. Krupovic, M. et al. *Virus Res.* **244**, 181–193 (2018).
5. Liu, Y. et al. *Nature* **593**, 553–557 (2021).
6. Bell, P. J. L. *Virus Res.* **289**, 198168 (2020).
7. Medvedeva, S. et al. *Nat. Microbiol.* https://doi.org/10.1038/s41564-022-01144-6 (2022).
8. Rambo, I. M. et al. *Nat. Microbiol.* https://doi.org/10.1038/s41564-022-01150-8 (2022).
9. Tamarit, D. et al. *Nat. Microbiol.* https://doi.org/10.1038/s41564-022-01122-y (2022).
10. Rahlff, J. et al. *Nat. Commun.* **12**, 4642 (2021).
11. Džunková, M. et al. *Nat. Microbiol.* **4**, 2192–2203 (2019).

Competing interests

The authors declare no competing interests.