Host range and cell recognition of archaeal viruses

Sensevdi, Emine Rabia; Sourrouille, Zaloa Aguirre; Quax, Tessa Ef

Published in:
Current Opinion in Microbiology

DOI:
10.1016/j.mib.2023.102423

Publication date:
2024

Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Microbiology

Host range and cell recognition of archaeal viruses

Emine Rabia Sensevdi*, Zaloa Aguirre Sourrouille* and Tessa EF Quax

Archaea are members of a separate domain of life that have unique properties, such as the composition of their cell walls and the structure of their lipid bilayers. Consequently, archaeal viruses face different challenges to infect host cells in comparison with viruses of bacteria and eukaryotes. Despite their significant impact on shaping microbial communities, our understanding of infection processes of archaeal viruses remains limited. Several receptors used by archaeal viruses to infect cells have recently been identified. The interactions between viruses and receptors are one of the determinants of the host range of viruses. Here, we review the current literature on host ranges of archaeal viruses and factors that might impact the width of these host ranges.

Address
Biology of Archaea and Viruses, Groningen Biomolecular Sciences and Biotechnology Institute, Faculty of Science and Engineering, University of Groningen, 9747 Groningen AG, the Netherlands

Corresponding author: Quax, Tessa EF (t.e.f.quax@rug.nl)
* These authors contributed equally to this work.

Current Opinion in Microbiology 2023, **77**:102423

This review comes from a themed issue on **Host-Microbe Interactions: viruses**

Edited by **Rob Lavigne** and **Julia Frunzke**

Available online xxxx

https://doi.org/10.1016/j.mib.2023.102423

Introduction

Archaea are ubiquitous microorganisms found across various ecosystems. They thrive in a wide range of environments, encompassing extreme habitats such as hot springs and hypersaline environments, as well as more moderate ones such as the ocean and the human body [1–5]. Archaea represent a significant part of the microbial diversity and are key players in various nutrient cycles [6–8]. Many archaea possess a pseudocrystalline proteinaceous surface layer called the S-layer, which provides both physical and chemical protection [9–11]. In addition to S-layers, other types of cell envelopes have been found in archaea such as pseudomurein, methanochondroitin, and protein sheaths (present in some methanogenic archaea) [12]. The archaeal cell envelope also contains filamentous appendages, which are involved in surface adhesion, cell–cell communication, DNA exchange, motility, and biofilm formation, and they represent an initial attachment site for some viruses [13–17].

Archaeal viruses

Archaeal viruses exhibit not only extraordinary morphological diversity but also an impressive genetic repertoire, with over 75% of their genes encoding unique proteins exclusive to these viruses [18]. Currently, archaeal viruses are classified into 33 families that can be divided into two groups: *(i)* archaea-specific (viruses with morphologies that are unique to archaea) and *(ii)* cosmopolitan archaeal viruses (viruses that are structurally similar to bacterial and eukaryotic viruses) [19–21]. All isolated archaeal viruses up to date infect members from two major phyla: *Thermoproteota* and *Euryarchaeota*. In addition, recent metagenomic studies have uncovered a spectrum of novel uncultivated archaeal viruses that have also been assigned to families [22–25]. Archaea-specific viruses display a remarkable array of morphologies, including spindle-shaped (*Bicaudaviridae*, *Fuselloviridae*, and *Halspiviridae*), bottle-shaped (*Ampullaviridae*), droplet-shaped virions (*Guttaviridae*), and filamentous-shaped virions (*Rudiviridae*, *Lipothrixviridae*, *Clavaviridae*, and *Tristromaviridae)* [18,19,26,27]. Most of the archaea-specific viruses infect hyperthermophilic archaea [18,27].

The cosmopolitan archaeal viruses, on the other hand, include head-tailed viruses of the order *Caudoviricetes* and the families *Sphaerolipoviridae* and *Turriviridae* [20,28]. All of these viruses, apart from the turriviruses, are known to infect members of *Euryarchaeota* [29,30].

First steps in viral infection

Viruses start their infection cycle by first attaching to a specific receptor on the surface of the host cell [31]. Next, the viral genome enters the host cell, either naked, leaving the protein capsid behind, or with the capsid. If the capsid enters the cell, an additional uncoating step is needed. Our knowledge on these first steps of the infection cycle, the host recognition and entry of archaeal viruses, is still rather scarce. Several studies have shown that most archaeal viruses studied up

Table 1

Host ranges and viral receptor complexes used by archaeal viruses.

Morphology	Family	Virus	Viral receptor complexes and receptors used by archaeal viruses	Host	Host range	Reference
Bottle-shaped	*Ampullaviridae*	ABV	Pointed end of the virions may be involved in attachment to membrane vesicles	*Acidianus* genus	Narrow	[34,36,37]
Filamentous	*Ungulaviridae* Genus: *Captovirus*	AFV1	Attaches to cellular pili via claw-like structures found at the distal end of the virion	*Acidianus hospitales*	Narrow	[38,39]
	Liphothrixviridae Genus: *Deltalipothrixvirus*	AFV2	Might attach to cellular pili via brush-like filamentous structures at the distal end of the virion	*Acidianus hospitales*	Extremely narrow	[34,39,40]
	Tristromaviridae Genus: *Alphatristromavirus*	PFV1	Possible entry through the use of heavily glycosylated host surface proteins	*Pyrobaculum arsenaticum*	Narrow	[27]
	Tristromaviridae Genus: *Betatristromavirus*	TTV1 TTV2	Possible entry through terminal filaments	*Thermoproteus tenax*	Narrow	[27,41]
	Rudiviridae Genus: *Hoswirudivirus*	SSRV1	Interacts with type-IV pili of *Saccharolobus solfataricus*	*Saccharolobus solfataricus*	Narrow	[42]
	Liphothrixviridae Genus: *Betalipothrixvirus*	SIFV	Potential attachment through a mop-like structure at its termini	*Sulfolobus islandicus*	Narrow (limited to a few *Sulfolobus* isolates of the *islandicus* type)	[43]
Head–tail	*Hafunaviridae* Genus: *Haloferacalesvirus*	HCTV-12	Adhesin-encoding genes may play an important role in determining host range, as has been shown for T-even phages. It is possible that they interact with glycans, just as T-even phages interact with lipopolysaccharides (LPS) on the bacterial membrane	14 different strains from 5 genera: *Halorubrum, Haloarcula, Halobacterium, Halobellus,* and *Haloterrigena*	Broad	[44-48]
	Hafunaviridae Genus*:* *Haloferacalesvirus*	HF1		HF1: Three genera*:* *Haloferax, Halobacterium,* and *Haloarcula*	Broad	[44–49]
	Haloferuviridae Genus: *Retbasiphovirus*	HFTV1	Attaches to cell wall component surface (S)-layer protein	*Haloferax gibbonsii* LR2–5	Extremely narrow	[32]
	Not defined	HRTV-DL1	Might probably bind to one of the two S-layer proteins	*Halorubrum lacusprofundi*	Narrow	[50,51]
	Vertoviridae Genus: *Myohalovirus*	ϕCh1	Attaches to galactose moieties on the surface of the host using its tail fibers	*Natrialba magadii*	Narrow	[47,52,53]
Icosahedral	*Turriviridae* Genus: *Alphaturrivirus*	STIV1 STIV2	Virions bind to highly flexible host filaments called 'thread' through a viral turret protein, although their identity is not known	*Sulfolobus Solfataricus Sulfolobus sp.*	Narrow	[54]
	Sphaerolipoviridae Genus: *Alphasphaero-lipovirus*	HCIV1	Possible attachment to host through spike complexes. Showed homology to SH1 major spike complex proteins	*Haloarcula californiae*	Narrow	[55-57]
	Sphaerolipoviridae Genus: *Alphasphaero-lipovirus*	HHIV2	Possible attachment to host through propeller-like spike structure	*Haloarcula hispanica*	Narrow	[56,58]
Pleomorphic	*Pleolipoviridae* Genus: *Alphapleolipovirus*	HRPV-1	Virus–host interactions are mediated by a sugar residue found at the host's S-layer protein and the virus capsid protein (N-formyl legionaminic)	*Halorubrum genus*	Narrow	[59]
	Pleolipoviridae Genus: *Alphapleolipovirus*	HRPV6	Enters via virus–cell membrane fusion with its VP4-like spike protein and the host membrane	*Halorubrum* genus	Narrow	[60]

Table 1 (*continued*)

Morphology	Family	Virus	Viral receptor complexes and receptors used by archaeal viruses	Host	Host range	Reference
	Globulaviridae Genus: *Alphaglobulavirus*	TSPV1	It contains highly unusual, glycosylated filaments on its surface. It was proposed that it recognizes the host via glycans	*Thermopro-teales* genus	Narrow	[61]
Rod-shaped	*Rudiviridae* Genus: *Icerudivirus*	SIRV2	Attaches to the pili on the surface of *Sulfolobus islandicus* LAL 14/1 through three terminal fibers. This virion might move along the pili toward the cell surface	*Sulfolobus islandicus*	Narrow	[16,35]
Spherical	*Sphaerolipoviridae* Genus: *Alphasphaero-lipovirus*	SH1	Possible attachment to host through horn-like spike structures	*Haloarcula hispanica*	Narrow	[58,62,63]
Spindle-shaped	*Bicaudaviridae* Genus: *Bicaudavirus*	ATV	It attaches with the minor protein p529 to the N-linked glycoprotein OppA (Ss) at the cell surface. The AAA ATPase (Adenosine triphosphatases Associated with diverse cellular Activities) may also trigger Acidianus two-tailed virus (ATV) host cell receptor recognition	*Acidianus* genus	Narrow	[63]
	Fuselloviridae Genus: *Alphafusellovirus*	SSV1	Short terminal fibers that might be involved in host recognition	*Sulfolobus* genus	Narrow	[34,64,65]
	Fuselloviridae Genus: *Betafusellovirus*	SSV6 ASV1	Three-to-four thick, slightly curved fibers show genomic features that suggest that they are composed of host-attachment proteins	*Sulfolobus* genus	Narrow	[34]

to date can either bind to the S-layer glycoproteins or to filamentous structures at the host surface [32,33]. The current knowledge on host receptors used by archaeal viruses is summarized in Table 1 (for a recent review, see Kuiper et al., 2024). As structure and function are closely linked for viruses, the morphological diversity of archaeal viruses suggests that entry mechanisms used by archaeal viruses could be very diverse as well [32–35]. The specificity of this virus-receptor interaction determines the range of hosts that can be infected by a particular virus [31].

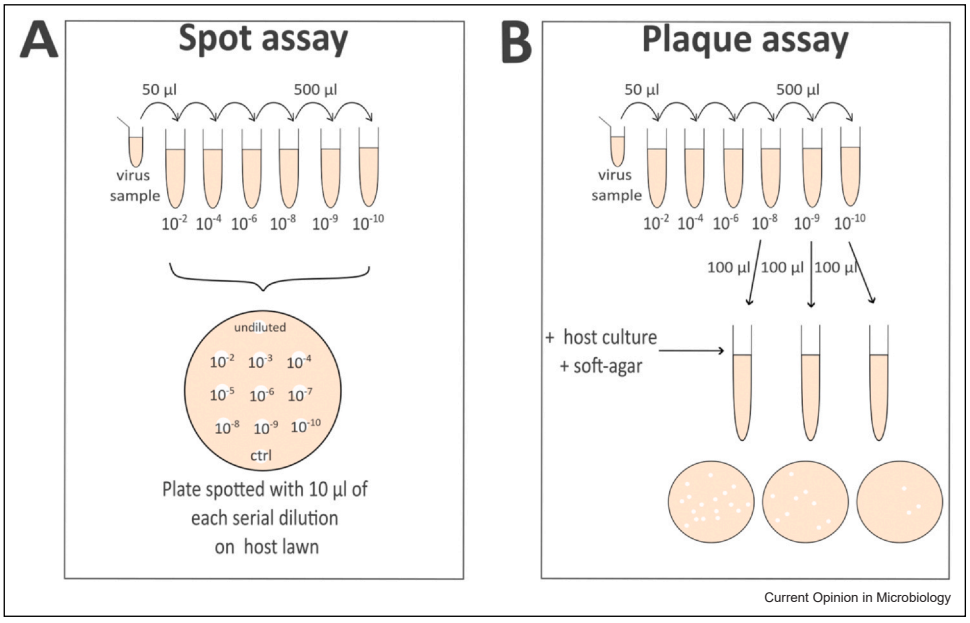
Description of host ranges

A virus' host range is the spectrum of cell types and host species a virus is able to infect and produce progeny virus from. The host range varies between different viruses. Some viruses are described to have broad host ranges, which means that these viruses can successfully infect multiple hosts, either multiple strains of the same species, or even different species or members of different genera [66,67]. The term 'narrow host range' is used for viruses that can only infect closely related strains/species. Viruses that can only infect a single host strain are often described as having an 'extremely narrow' host range.

Some factors that impact the virus–host range include *(i)* viral binding to host receptors, *(ii)* successful genome delivery (i.e. help in particle uncoating), *(iii)* availability of the requirements for replication (i.e. a host-encoded polymerase), *(iv)* virus-resistance mechanisms encoded by the host, such as the Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein 9 (CRISPR/Cas) system, and *(v)* the modularity of the phage–host interaction networks [44,68–70]. Viruses can either bind to a specific conserved receptor (monovalent viruses) or multiple distinct receptors (polyvalent viruses) [66,44,71]. From bacteriophages, it is known that monovalent broad host range viruses use conserved receptors that are present across multiple hosts, whereas polyvalent broad host range bacteriophages usually are able to bind to multiple distinct receptors [44]. For example, the bacteriophages ϕ92 and SP6 have been shown to encode multiple receptor-binding proteins (RBPs), as part of their capsid, with different receptor specificities [72,73].

Host ranges can be determined with the help of laboratory techniques. Traditional methods, such as plaque assay or spot-on-lawn assays, are widely used for viruses that form plaques on a host lawn (Figure 1). In contrast, non-lytic viruses can be identified by quantitative Polymerase Chain Reaction (qPCR) (Figure 2**c**). New techniques such as historical virus encounter tracing via CRISPR arrays, single-cell genomics, and viral tagging now allow exploration of viral host ranges with

Figure 1



Laboratory techniques used to determine the host ranges of plaque-forming viruses. **(a)** *Spot assay*. A dilution series of each virus is prepared and drops of each dilution are spotted on a lawn of cells (known or potential host cell). The plates are incubated and examined for the presence of zones of clearance due to lysis or growth inhibition. **(b)** *Plaque assay*. Different dilutions of virus sample are mixed with the host culture and melted top layer agar and plated on a solid plate to quantify the number of infectious particles on a host lawn.

uncultured viruses or host strains (Figure 2) [74,75]. When comparing the host range of viruses, it is important to consider the method used to determine the host range, as experiments performed under laboratory conditions might only reveal part of the full host range that viruses display in their natural environment [75]. Therefore, it is important to always mention the technique that was used to determine host range, and ideally use multiple complementary techniques to determine host ranges. Additional computational techniques can also be used to determine the host ranges of uncultivated viruses either based on their host(s) sequences or comparing virus genomes to the genomes of other viruses of which the host(s) are known [76,77]. In addition, it is important to keep in mind that host ranges are fluid and change over time. Receptors recognized by viruses might be expressed only under certain conditions (e.g. certain receptors might only be expressed at specific growth phases), and the incorporation of a new spacer in the CRISPR array can suddenly render a strain resistance to a certain virus. Thus, a viral host range is not a strongly defined list of species, but it is dependent on both the method used to determine it and also on the growth conditions of the host cells.

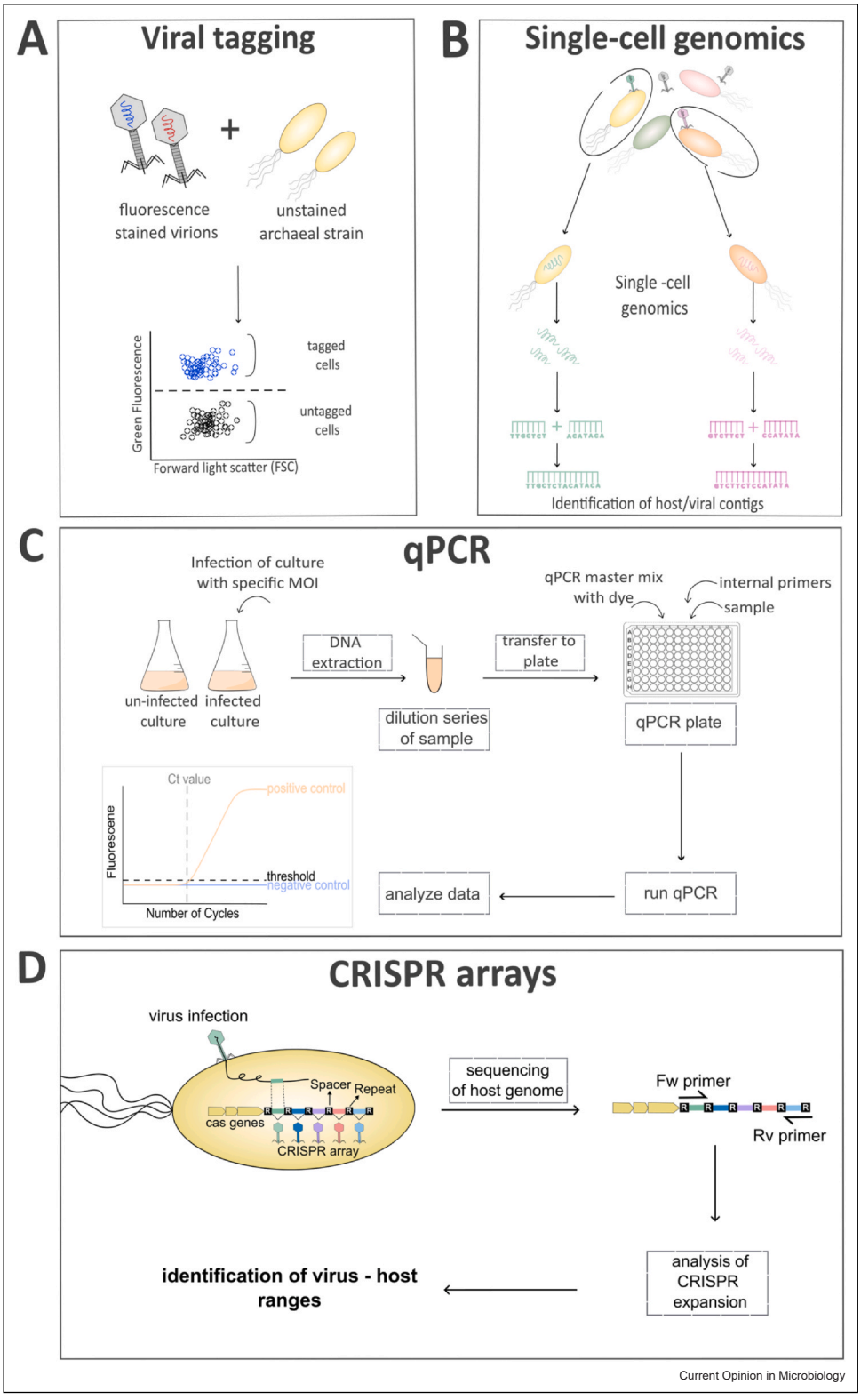
Members of many archaeal phyla and their viruses have not been cultivated yet. Thus, it has to be taken into account that the information on host ranges is still limited. However, with the cultivation-independent methods described above, we expect a great leap forward in this field in the years to come. Viral tagging has thus far not been applied to archaeal systems, but has great potential to significantly increase knowledge on archaeal virus–host ranges.

Host ranges of archaeal viruses

The host ranges of archaeal viruses can vary from extremely narrow (1–2 hosts) to broad (multiple taxonomically distinct hosts) (Figure 3) [20,74,78]. In a study conducted by Ceballos et al., the host ranges of various Sulfolobus spindle-shaped viruses (SSVs), namely SSV1, SSV2, SSV3, SSVL1, SSVK1, and SSVRH, were examined [74,79]. The investigation employed spot-on-lawn assays and encompassed multiple hosts from the *Sulfolobaceae* family. The results unveiled that SSV1 exhibited the narrowest host range, exclusively infecting *Sulfolobus solfataricus* strains P1 and P2, while failing to infect *Sulfolobus acidocaldarius* [64]. Conversely, SSVRH demonstrated the broadest host range, infecting hosts beyond the *Sulfolobus* genus [74]. In a more recent investigation by Iverson et al., it was shown that deletion of the viral integrase of SSV1 led to an alteration of the host range by an unknown mechanism [80].

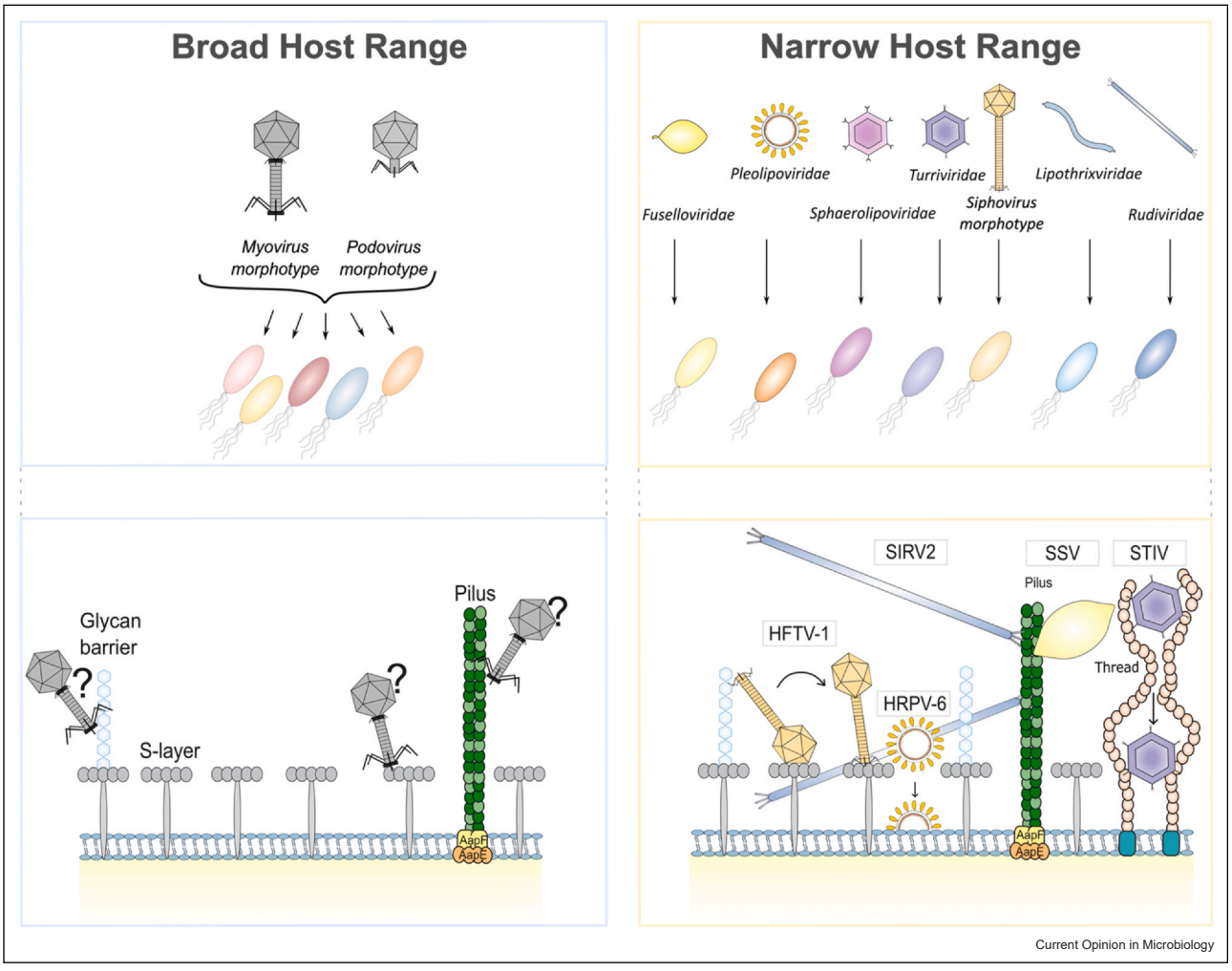
Pleomorphic viruses such as HHPV-3 and HHPV-4 exhibited a narrow host range, as demonstrated in plaque and spot-on-lawn assays conducted on 47 haloarchaeal strains

Figure 2


A
Viral tagging
fluorescence stained virions
unstained archaeal strain
Green Fluorescence
tagged cells
untagged cells
Forward light scatter (FSC)
B
Single-cell genomics
Single -cell genomics
Identification of host/viral contigs
C
qPCR
Infection of culture with specific MOI
un-infected culture
infected culture
DNA extraction
dilution series of sample
transfer to plate
qPCR master mix with dye
internal primers
sample
qPCR plate
run qPCR
analyze data
Ct value
positive control
threshold
negative control
Fluorescene
Number of Cycles
D
CRISPR arrays
virus infection
Spacer
Repeat
cas genes
CRISPR array
sequencing of host genome
Fw primer
Rv primer
analysis of CRISPR expansion
identification of virus - host ranges
Current Opinion in Microbiology

Laboratory techniques used to determine the host ranges of non-plaque-forming viruses. **(a)** *Viral tagging*. Viruses are labeled with DNA-binding fluorescent dyes and mixed with potential host strains. The samples are then sorted using a flow cytometer. The scatterplot shows the expected positions of the fluorescently labeled (viral-tagged, shown in blue) and unlabeled (nontagged, shown in black) cells. The analysis of viral DNA by genomic sequencing provides further information about the viruses and their host range. **(b)** *Single-cell genomics*. It is used to study the genetic information within a single cell (uninfected or infected cells). Hereby, single cells are isolated and the whole DNA within the isolated cell is amplified and analyzed by next-generation DNA sequencing. This technique enables the study of viral host range by linking virus and host genomes that reside in the same cell. **(c)** *qPCR*. This method can be used to detect viruses, such as chronic viruses that do not form visible plaques or spots on a host lawn. qPCR is a real-time DNA detection method that can be used to detect viral DNA in host populations. Cultures are infected with virus, washed and incubated, and after harvest, the presence of intracellular viral DNA is quantified with qPCR. **(d)** *CRISPR arrays*. This technique enables identification of historical virus by analyzing specific spacer sequences stored within the host's genome. When a host cell, equipped with a CRISPR–Cas system, encounters a virus, Cas proteins capture a segment of the viral DNA, integrating it as a new spacer at one end of the CRISPR array. By sequencing the CRISPR array in the host genome, recent virus encounters can be detected by spacer acquisitions close to the leader sequence. This method can also be applied for viruses that are not yet isolated. Each spacer's distinct color signifies a different acquired virus DNA.

Figure 3



Schematic representation of archaeal virus–host ranges viral binding. The upper panel illustrates archaeal viruses with a broad (left upper side, highlighted in blue) and narrow (right upper side, highlighted in yellow) host range. Different colors are used for distinct archaeal host strains. The lower panel details the interaction of certain archaeal viruses with the host cell surface and the receptors involved in attachment. The question mark indicates yet-undiscovered receptors (left lower panel). Viruses and the cell surface are not drawn to scale.
This figure is adapted from reference [33].

[78,81]. Similarly, HRPV-1 displayed plaques exclusively on *Halorubrum sp*. PV6 after being tested on 13 haloarchaeal strains by spot-on-lawn assays [82]. The pleolipovirus SNJ2 also exhibited a narrow host range [55]. Thus, generally pleolipoviruses tend to have narrow host ranges. One exception is the recently isolated HFPV-1, which was shown to display a board host range [83]. Sphaerolipoviruses have also been associated with narrow host ranges, although it has been postulated that SH1 and PH1 in their natural environment might infect a broader range of hosts than observed under laboratory conditions [56].

The archaeal tailed viruses (arTVs), which are morphologically similar to tailed bacteriophages of the class *Caudoviricetes*, show different host ranges in comparison to pleolipoviruses and sphaerolipoviruses (Figure 3) [20]. While some of the members infect a single isolate, others can infect several species from different haloarchaeal genera and have thus a broad host range. For example, broad host ranges were observed for myovirus-like viruses infecting *Halorubrum*, particularly HCTV-12 [29,45]. To gain insight into the factors influencing the diverse host ranges observed in arTVs, spot-on-lawn and plaque assays were conducted with viruses of the family *Hafunaviridae* [20]. Hafunaviruses, which are known for their broad host ranges, represent the largest family of myovirus-like archaeal viruses. Liu et al. found that two adjacent genes located at the end-of-the-tail morphogenesis module play a role in host specificity [20]. One of the two genes encodes a glycine-rich protein, while the other gene encodes a small putative protein. The glycine-rich protein possesses typical features observed in adhesin proteins found at the distal tip of the tail fiber in various T-even bacteriophages, which enables recognition of diverse host receptors [20,45]. Thus, adhesin-encoding genes could serve as crucial determinants for host range specificity in Hafunaviruses. Despite the differences in the cell surface structures of archaea and bacteria, the tail adhesins exhibit striking sequence similarities between arTVs and myophages, with four hypervariable segments separated by a set of highly conserved glycine-rich motifs [20,46].

Furthermore, it has been shown that archaeal viruses exchange host-specific genetic modules for RBPs, enhancing their ability to infect a broad range of host strains [20]. The high sequence divergence in certain regions of Hafunavirus' adhesins likely allows these viruses to interact with a wide array of receptor molecules on the host surface, contributing to their competitiveness in environments with high virus-to-host ratios.

Conclusion

Recently, the host range of a select group of archaeal viruses has been determined. In general, archaeal sphaerolipoviruses and pleolipoviruses often have narrow host ranges, while myovirus-like archaeal viruses infect a wider range of hosts. Still, the variation in host range width between members of the same family can be very big and, thus, the viral taxonomy cannot be used solely as a prediction of host range width.

The host range of bacterial and eukaryotic viruses is known to depend on various factors, including its binding to the host receptor, the virion morphology, host defense systems, and the entry and exit mechanisms.

The factors determining the host range remain obscure for most archaeal viruses. The only exception are the adhesins at the distal tip of the tail fibers that were reported to play a role in the host range of arTVs [20]. For bacterial head–tail viruses, the ability to interact with their host is mediated by RBPs including tail fibers, tailspikes and tail tips. The majority of bacteriophages express a single RBP, but certain phages express multiple RBPs. These diverse RBPs can recognize distinct receptors, enabling the phages to infect a variety of hosts**.** For example Klebsiella jumbo myophage ϕKp24 has 15 different tail fibers [84]. In the genomes of arTVs, a single gene encoding a tail fiber is present. However, as for the large majority of archaeal viruses their RBPs have not been identified yet, it might be possible that some viruses with different morphologies do encode multiple RBPs, similarly to bacteriophages with multiple RBPs, which could allow them to broaden their host ranges.

The interaction between RBPs and viral receptors at the cell surface could be one of the most pronounced host range determinants, as this is the very first step of the infection cycle. For a select group of archaeal viruses (Table 1), the RBPs have been determined, such as the tail fibers of arTVs or the appendages at the ends of lipotrixviruses. Some of these (un)identified RBPs might have more mutational 'freedom' than others if they are not required for the stability of the virus, enabling them to expand their host range.

Not only the RBPs are important for host recognition, but also the receptors on the host cell surface. Both the S-layer and the filamentous surface structures were already identified as viral receptors (Table 1). It has been shown that genes encoding archaeal surface filaments, such as T4P, are horizontally transferred between different archaea. This horizontal gene transfer contributes to the diversity of the cell surface among archaeal species. Transfer of receptors to new archaea, will affect the host range of viruses using these receptors. Moreover, several archaea, such as haloarchaea, encode multiple copies of their cell surface components, such as S-layer proteins, archaellins (the main component of the archaellum), or pilins (the major component of adhesive T4P). Some of these have been suggested to function as ecoparalogs, genes that perform similar functions under different environmental conditions. It is not yet studied in detail under which conditions the

different gene copies of these cell surface genes are expressed. The growth phase or environmental conditions likely affect the expression of these viral receptors, which in turn will impact the viral host range.

In eukaryotic viruses, host range determinants and explanations for host species jumps are an important field of research. Influenza-A virus, for example, can rapidly expand its host range and adapt to new species, as it can undergo extensive reassortment of their genes when different viruses infect a single cell simultaneously. Structural features of the host glycoconjugates also affect the interactions of influenza virus and its receptor. This genomic reassortment as for influenzamight be difficult in archaeal viruses, as their genomes are not segmented. However, infection of one cell by multiple viruses has been reported for archaea and thus might enhance the exchange of genetic modules responsible for virion architecture, replication, or release [13,19].

It is important to understand how viruses and hosts coevolve in response to each other, as viral host ranges profoundly impact ecosystems and expanding host ranges can cause viral epidemics among different hosts (e.g. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, Ebola outbreaks, and demise of algal blooms). Although for archaea we do not speak about 'disease,' infection still can lead to profound cell dysfunctioning or even cell death. Changing host ranges could result in potential virus 'epidemic' in archaea.

Studying host range determinants in archaea, and the comparison of these with similar studies for bacterial and eukaryotic viruses, will allow the detection of universal factors impacting viral host range. This insight into viral host range determinants is important to predict and monitor the development of cell disfunctioning and the balance in many ecosystems.

In the years to come, the increased application of viral-tagging and single-cell genomics will likely significantly expand the number of characterized archaeal virus–host ranges. In combination with mechanistic laboratory studies, we anticipate many interesting findings in this relatively new field of research.

Authors' contributions

T.E.F.Q, Z.A.S., and E.R.S.: conceptualization. T.E.F.Q.: funding acquisition. Z.A.S. and E.R.S.: writing original draft. All authors contributed to the writing and editing of the paper. All authors have read and agreed to the paper.

Data Availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by funding from the Hector Fellow Academy to T.E.F.Q. and Z.A.S. and E.R.S. This work received funding from the European Research Council (ERC) (101039446 ARCVIR).

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Kim JY, Whon TW, Lim MY, Kim YB, Kim N, Kwon MS, Kim J, Lee SH, Choi HJ, Nam IH, *et al.*: **The human gut archaeome: identification of diverse haloarchaea in Korean subjects**. *Microbiome* 2020, **8**:114.
2. Eme L, Doolittle WF: **Archaea**. *Curr Biol* 2015, **25**:R851-R855.
3. Blohs M, Moissl-Eichinger C, Mahnert A, Spang A, Dombrowski N, Krupovic M, Klingl A: **Archaea-an introduction**. Encyclopedia of Microbiology. Elsevier; 2019:243-252.
4. Wang H, Bier R, Zgleszewski L, Peipoch M, Omondi E, Mukherjee A, Chen F, Zhang C, Kan J: **Distinct distribution of archaea from soil to freshwater to estuary: implications of archaeal composition and function in different environments**. *Front Microbiol* 2020, **11**:576661.
5. Hoegenauer C, Hammer HF, Mahnert A, Moissl-Eichinger C: **Methanogenic archaea in the human gastrointestinal tract**. *Nat Rev Gastroenterol Hepatol* 2022, **19**:805-813.
6. De Lise F, Iacono R, Moracci M, Strazzulli A, Cobucci-Ponzano B: **Archaea as a model system for molecular biology and biotechnology**. *Biomolecules* 2023, **13**:114.
7. Baker BJ, De Anda V, Seitz KW, Dombrowski N, Santoro AE, Lloyd KG: **Diversity, ecology and evolution of Archaea**. *Nat Microbiol* 2020, **5**:887-900.
8. Spang A, Ettema TJG: **Archaeal evolution: the methanogenic roots of Archaea**. *Nat Microbiol* 2017, **2**:17109.
9. Sleytr UB, Schuster B, Egelseer EM, Pum D: **S-layers: principles and applications**. *FEMS Microbiol Rev* 2014, **38**:823-864.
10. Rodrigues-Oliveira T, Belmok A, Vasconcellos D, Schuster B, Kyaw CM: **Archaeal S-layers: overview and current state of the art**. *Front Microbiol* 2017, **8**:2597.
11. Pohlschroder M, Pfeiffer F, Schulze S, Halim MFA: **Archaeal cell surface biogenesis**. *FEMS Microbiol Rev* 2018, **42**:694-717.
12. Albers SV, Meyer BH: **The archaeal cell envelope**. *Nat Rev Microbiol* 2011, **9**:414-426.
13. Munson-Mcgee JH, Peng S, Dewerff S, Stepanauskas R, Whitaker RJ, Weitz JS, Young MJ: **A virus or more in (nearly) every cell: ubiquitous networks of virus-host interactions in extreme environments**. *ISME J* 2018, **12**:1706-1714.
14. Chaudhury P, Quax TEF, Albers SV: **Versatile cell surface structures of archaea**. *Mol Microbiol* 2018, **107**:298-311.
15. Klingl A, Pickl C, Flechsler J: **Archaeal cell walls**. *Subcell Biochem* 2019, **92**:471-493.
16. Deng L, He F, Bhoobalan-Chitty Y, Martinez-Alvarez L, Guo Y, Peng X: **Unveiling cell surface and type IV secretion proteins responsible for archaeal rudivirus entry**. *J Virol* 2014, **88**:10264-10268.

17. Jarrell KF, Ding Y, Nair DB, Siu S: **Surface appendages of archaea: structure, function, genetics and assembly**. *Life: Open Access J* 2013, **3**:86.

18. Krupovic M, Cvirkaite-Krupovic V, Iranzo J, Prangishvili D, Koonin EV: **Viruses of archaea: structural, functional, environmental and evolutionary genomics**. *Virus Res* 2018, **244**:181-193.

19. •• Baquero DP, Liu Y, Wang F, Egelman EH, Prangishvili D, Krupovic M: **Structure and assembly of archaeal viruses**. *Adv Virus Res* 2020, **108**:127-164.
Excellent review providing an overview of the structure and characteristics of archaeal viruses.

20. •• Liu Y, Demina TA, Roux S, Aiewsakun P, Kazlauskas D, Simmonds P, Prangishvili D, Oksanen HM, Krupovic M: **Diversity, taxonomy, and evolution of archaeal viruses of the class Caudoviricetes**. *PLoS Biol* 2021, **19**:e3001442.
This study focuses on host-range determinants of the archaeal viruses of the class *Caudoviricetes*.

21. Wirth J, Young M: **The intriguing world of archaeal viruses**. *PLoS Pathog* 2020, **16**:e1008574.

22. Medvedeva S, Sun J, Yutin N, Koonin EV, Nunoura T, Rinke C, Krupovic M: **Three families of Asgard archaeal viruses identified in metagenome-assembled genomes**. *Nat Microbiol* 2022, **7**:962-973.

23. Zhou Y, Zhou L, Yan S, Chen L, Krupovic M, Wang Y: **Diverse viruses of marine archaea discovered using metagenomics**. *Environ Microbiol* 2023, **25**:367-382.

24. Li R, Wang Y, Hu H, Tan Y, Ma Y: **Metagenomic analysis reveals unexplored diversity of archaeal virome in the human gut**. *Nat Commun 2022 13:1* 2022, **13**:1-12.

25. Rambo IM, Langwig MV, Leão P, De Anda V, Baker BJ: **Genomes of six viruses that infect Asgard archaea from deep-sea sediments**. *Nat Microbiol* 2022, **7**:953-961, https://doi.org/10.1038/s41564-022-01150-8

26. Liu Y, Du S, Chen X, Dyall-Smith M, Jalasvuori M, Oksanen HM, Siddell SG, Lefkowitz EJ, Sabanadzovic S, Simmonds P, *et al*.: **ICTV virus taxonomy profile: simuloviridae 2023**. *J Gen Virol* 2023, **104**:911-912.

27. Rensen EI, Mochizuki T, Quemin E, Schouten S, Krupovic M, Prangishvili D: **A virus of hyperthermophilic archaea with a unique architecture among DNA viruses**. *Proc Natl Acad Sci USA* 2016, **113**:2478-2483.

28. Demina TA, Dyall-Smith M, Jalasvuori M, Du S, Oksanen HM: **ICTV virus taxonomy profile: sphaerolipoviridae 2023**. *J Gen Virol* (3) 2023, **104**:p001830001830.

29. Aguirre Sourrouille Z, Schwarzer S, Lequime S, Oksanen HM, Quax TEF: **The viral susceptibility of the Haloferax species**. *Viruses* 2022, **14**:1344.

30. Pietilä MK, Laurinmäki P, Russell DA, Ko C-C, Jacobs-Sera D, Butcher SJ, Bamford DH, Hendrix RW: **Insights into head-tailed viruses infecting extremely halophilic archaea**. *J Virol* 2013, **87**:3248-3260.

31. Maginnis MS: **Virus–receptor interactions: the key to cellular invasion**. *J Mol Biol* 2018, **430**:2590.

32. Schwarzer S, Hackl T, Oksanen HM, Quax TEF: **Archaeal host cell recognition and viral binding of HFTV1 to its Haloferax host**. *mBio* 2023, **14**:e0183322.

33. • Tittes C, Schwarzer S, Quax TEF: **Viral hijack of filamentous surface structures in archaea and bacteria**. *Viruses* 2021, **13**:164.
This review provides an overview of different surface structures of the archaeal and bacterial cell envelope that can be used by a viruses for attachment and infection.

34. Quemin ERJ, Quax TEF: **Archaeal viruses at the cell envelope: entry and egress**. *Front Microbiol* 2015, **6**:552.

35. Quemin ERJ, Lucas S, Daum B, Quax TEF, Kühlbrandt W, Forterre P, Albers S-V, Prangishvili D, Krupovic M: **First insights into the entry process of hyperthermophilic archaeal viruses**. *J Virol* 2013, **87**:13379-13385.

36. Atanasova NS, Roine E, Oren A, Bamford DH, Oksanen HM: **Global network of specific virus-host interactions in hypersaline environments**. *Environ Microbiol* 2012, **14**:426-440.

37. Peng X, Basta T, Häring M, Garrett RA, Prangishvili D: **Genome of the Acidianus bottle-shaped virus and insights into the replication and packaging mechanisms**. *Virology* 2007, **364**:237-243.

38. Basta T, Smyth J, Forterre P, Prangishvili D, Peng X: **Novel archaeal plasmid pAH1 and its interactions with the lipothrixvirus AFV1**. *Mol Microbiol* 2009, **71**:23-34.

39. Bettstetter M, Peng X, Garrett RA, Prangishvili D: **AFV1, a novel virus infecting hyperthermophilic archaea of the genus Acidianus**. *Virology* 2003, **315**:68-79.

40. Häring M, Rachel R, Peng X, Garrett RA, Prangishvili D: **Viral diversity in hot springs of Pozzuoli, Italy, and characterization of a unique archaeal virus, acidianus bottle-shaped virus, from a new family, the Ampullaviridae**. *J Virol* 2005, **79**:9904-9911.

41. Janekovic D, Wunderl S, Holz I, Zillig W, Gierl A, Neumann H: **TTV1, TTV2 and TTV3, a family of viruses of the extremely thermophilic, anaerobic, sulfur reducing archaebacterium Thermoproteus tenax**. *MGG Mol Gen Genet* 1983, **192**:39-45.

42. Wang F, Baquero DP, Su Z, Beltran LC, Prangishvili D, Krupovic M, Egelman EH: **The structures of two archaeal type IV pili illuminate evolutionary relationships**. *Nat Commun* 2020, **11**:3424.

43. Arnold HP, Zillig W, Ziese U, Holz I, Crosby M, Utterback T, Weidmann JF, Kristjanson JK, Klenk HP, Nelson KE, *et al*.: **A novel lipothrixvirus, SIFV, of the extremely thermophilic crenarchaeon Sulfolobus**. *Virology* 2000, **267**:252-266.

44. •• De Jonge PA, Nobrega FL, Brouns SJJ, Dutilh BE: **Molecular and evolutionary determinants of bacteriophage host range**. *Trends Microbiol* 2019, **27**:51-63.
This study suggests that RBPs are an important factor determining the broad host range of some tailed bacterial viruses.

45. Atanasova NS, Demina TA, Buivydas A, Bamford DH, Oksanen HM: **Archaeal viruses multiply: temporal screening in a solar saltern**. *Viruses* 2015, **7**:1902.

46. Trojet SN, Caumont-Sarcos A, Perrody E, Comeau AM, Krisch HM: **The gp38 adhesins of the T4 superfamily: a complex modular determinant of the phage's host specificity**. *Genome Biol Evol* 2011, **3**:674.

47. Li Y, Liu D, Wang Y, Su W, Liu G, Dong W: **The importance of glycans of viral and host proteins in enveloped virus infection**. *Front Immunol* 2021, **12**:638573.

48. Rossmann MG, Mesyanzhinov VV, Arisaka F, Leiman PG: **The bacteriophage T4 DNA injection machine**. *Curr Opin Struct Biol* 2004, **14**:171-180.

49. Dyall-Smith M, Tang SL, Russ B, Chiang PW, Pfeiffer F: **Comparative genomics of two new HF1-like haloviruses**. *Genes* 2020, **11**:405.

50. Mercier C, Thies D, Zhong L, Raftery MJ, Erdmann S: **Characterization of an archaeal virus-host system reveals massive genomic rearrangements in a laboratory strain**. *Frontiers in Microbiology* 2023, **14**:1274068.

51. Mercier C, Thies D, Zhong L, Raftery MJ, Erdmann S: **Characterization of an archaeal virus-host system reveals massive genomic rearrangements in a laboratory strain**. *Frontiers in Microbiology* 2023, **14**.

52. Klein R, Rössler N, Iro M, Scholz H, Witte A: **Haloarchaeal myovirus φCh1 harbours a phase variation system for the production of protein variants with distinct cell surface adhesion specificities**. *Mol Microbiol* 2012, **83**:137-150.

53. Dyall-Smith M, Pfeifer F, Witte A, Oesterhelt D, Pfeiffer F: **Complete genome sequence of the model halovirus PhiH1 (ΦH1)**. *Genes* 2018, **9**:493.

54. Hartman R, Eilers BJ, Bollschweiler D, Munson-McGee JH, Engelhardt H, Young MJ, Lawrence CM: **The molecular**

mechanism of cellular attachment for an archaeal virus. *Structure* 2019, **27**:1634-1646.e3.

55. Demina TA, Oksanen HM: **Pleomorphic archaeal viruses: the family Pleolipoviridae is expanding by seven new species**. *Arch Virol* 2020, **165**:2723-2731.

56. Demina TA, Pietilä MK, Svirskaitė J, Ravantti JJ, Atanasova NS, Bamford DH, Oksanen HM: **HCIV-1 and other tailless icosahedral internal membrane-containing viruses of the family Sphaerolipoviridae**. *Viruses* 2017, **9**:32.

57. Demina TA, Pietilä MK, Svirskaitė J, Ravantti JJ, Atanasova NS, Bamford DH, Oksanen HM: **Archaeal haloarcula californiae icosahedral virus 1 highlights conserved elements in icosahedral membrane-containing DNA viruses from extreme environments**. *mBio* 2016, **7**:e00699-16.

58. Jaakkola ST, Penttinen RK, Vilén ST, Jalasvuori M, Rönnholm G, Bamford JKH, Bamford DH, Oksanen HM: **Closely related archaeal Haloarcula hispanica icosahedral viruses HHIV-2 and SH1 have nonhomologous genes encoding host recognition functions**. *J Virol* 2012, **86**:4734-4742.

59. Zaretsky M, Roine E, Eichler J: **Sialic acid-like sugars in archaea: legionaminic acid biosynthesis in the halophile Halorubrum sp. PV6**. *Front Microbiol* 2018, **9**:2133.

60. Bignon EA, Chou KR, Roine E, Tischler ND: **Halorubrum pleomorphic virus-6 membrane fusion is triggered by an S-layer component of its haloarchaeal host**. *Viruses* 2022, **14**:254.

61. Hartman R, Biewenga L, Munson-McGee J, Refai M, Boyd ES, Bothner B, Lawrence CM, Young M: **Discovery and characterization of thermoproteus spherical piliferous virus 1: a spherical archaeal virus decorated with unusual filaments**. *J Virol* 2020, **94**:e00036-20.

62. Jäälinoja HT, Roine E, Laurinmäki P, Kivelä HM, Bamford DH, Butcher SJ: **Structure and host-cell interaction of SH1, a membrane-containing, halophilic euryarchaeal virus**. *Proc Natl Acad Sci USA* 2008, **105**:8008-8013.

63. Erdmann S, Scheele U, Garrett RA: **AAA ATPase p529 of Acidianus two-tailed virus ATV and host receptor recognition**. *Virology* 2011, **421**:61-66.

64. Schleper C, Kubo K, Zillig W: **The particle SSV1 from the extremely thermophilic archaeon Sulfolobus is a virus: demonstration of infectivity and of transfection with viral DNA**. *Proc Natl Acad Sci USA* 1992, **89**:7645-7649.

65. Stedman KM, DeYoung M, Saha M, Sherman MB, Morais MC: **Structural insights into the architecture of the hyperthermophilic fusellovirus SSV1**. *Virology* 2015, **474**:105-109.

66. • Rothenburg S, Brennan G: **Species-specific host-virus interactions: implications for viral host range and virulence**. *Trends Microbiol* 2020, **28**:46.
This study explains implications for viral host range and virulence.

67. Bandín I, Dopazo CP: **Host range, host specificity and hypothesized host shift events among viruses of lower vertebrates**. *Vet Res* 2011, **42**:67.

68. Göller PC, Elsener T, Lorgé D, Radulovic N, Bernardi V, Naumann A, Amri N, Khatchatourova E, Coutinho FH, Loessner MJ, *et al.*: **Multi-species host range of staphylococcal phages isolated from wastewater**. *Nat Commun 2021 12:1* 2021, **12**:1-17.

69. Kauffman KM, Chang WK, Brown JM, Hussain FA, Yang J, Polz MF, Kelly L: **Resolving the structure of phage–bacteria interactions in the context of natural diversity**. *Nat Commun* 2022, **13**:1-20.

70. Flores CO, Valverde S, Weitz JS: **Multi-scale structure and geographic drivers of cross-infection within marine bacteria and phages**. *ISME J* 2012, **7**:520-532.

71. Hyman P, Abedon ST: **Bacteriophage host range and bacterial resistance**. *Adv Appl Microbiol* 2010, **70**:217-248.

72. Tu J, Park T, Morado DR, Hughes KT, Molineux IJ, Liu J: **Dual host specificity of phage SP6 is facilitated by tailspike rotation**. *Virology* 2017, **507**:206-215.

73. Schwarzer D, Buettner FFR, Browning C, Nazarov S, Rabsch W, Bethe A, Oberbeck A, Bowman VD, Stummeyer K, Mühlenhoff M, *et al.*: **A multivalent adsorption apparatus explains the broad host range of phage phi92: a comprehensive genomic and structural analysis**. *J Virol* 2012, **86**:10384-10398.

74. •• Ceballos RM, Marceau CD, Marceau JO, Morris S, Clore AJ, Stedman KM: **Differential virus host-ranges of the Fuselloviridae of hyperthermophilic Archaea: implications for evolution in extreme environments**. *Front Microbiol* 2012, **3**:26572.
In this study, the authors have tested the host ranges of archaeal viruses from the family *Fuselloviridae*.

75. Fong K, Wong CWY, Wang S, Delaquis P: **How broad is enough: the host range of bacteriophages and its impact on the agri-food sector**. *PHAGE: Ther, Appl, Res* 2021, **2**:83-91.

76. Roux S, Camargo AP, Coutinho FH, Dabdoub SM, Dutilh BE, Nayfach S, Tritt A: **iPHoP: an integrated machine learning framework to maximize host prediction for metagenome-derived viruses of archaea and bacteria**. *PLoS Biol* 2023, **21**:e3002083.

77. Edwards RA, McNair K, Faust K, Raes J, Dutilh BE: **Computational approaches to predict bacteriophage–host relationships**. *FEMS Microbiol Rev* 2016, **40**:258-272.

78. Atanasova NS, Heiniö CH, Demina TA, Bamford DH, Oksanen HM: **The unexplored diversity of pleolipoviruses: the surprising case of two viruses with identical major structural modules**. *Genes* 2018, **9**:131.

79. Rowland EF, Bautista MA, Zhang C, Whitaker RJ: **Surface resistance to SSVs and SIRVs in pilin deletions of Sulfolobus islandicus**. *Mol Microbiol* 2020, **113**:718.

80. Iverson EA, Goodman DA, Gorchels ME, Stedman KM: **Extreme mutation tolerance: nearly half of the archaeal fusellovirus sulfolobus spindle-shaped virus 1 genes are not required for virus function, including the minor capsid protein gene vp3**. *J Virol* 2017, **91**:e02406-16.

81. Demina TA, Atanasova NS, Pietilä MK, Oksanen HM, Bamford DH: **Vesicle-like virion of Haloarcula hispanica pleomorphic virus 3 preserves high infectivity in saturated salt**. *Virology* 2016, **499**:40-51.

82. Pietilä MK, Roine E, Paulin L, Kalkkinen N, Bamford DH: **An ssDNA virus infecting archaea: a new lineage of viruses with a membrane envelope**. *Mol Microbiol* 2009, **72**:307-319.

83. Alarcon-Schumacher T, Naor A, Gophna U, Erdmann S: **Isolation of a virus causing a chronic infection in the archaeal model organism Haloferax volcanii reveals antiviral activities of a provirus**. *Proc Natl Acad Sci USA* 2022, **119**:e2205037119.

84. Ouyang R, Costa AR, Cassidy CK, Otwinowska A, Williams VCJ, Latka A, Stansfeld PJ, Drulis-Kawa Z, Briers Y, Pelt DM, *et al.*: **High-resolution reconstruction of a Jumbo-bacteriophage infecting capsulated bacteria using hyperbranched tail fibers**. *Nat Commun* 2022, **13**:1-16.