

The Legacy of Viral Predation on Phage-Host Interaction Identification and Amgs

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Abstract

Viruses are the most abundant life form on earth and have been reported to have vital ecological roles, regulating the abundance and diversity of their hosts (i.e. bacteria and archaea). The relationship between phages and their hosts has been identified in silicon based on CRISPR or tRNA related approached. In-depth genome analysis of viruses has revealed multiple Auxiliary metabolic genes (AMGs) in phage genomes which are able to repurpose host metabolism.

Keywords

Viral predation, phage infection, ecological roles.

1. ECOLOGICAL ROLES OF PHAGES

Viruses have been reported to overwhelmingly dominate every environment. The fact that phages outnumber their hosts, with the virus-to-microbe ratio being approximate 10, was firstly reported in marine environments by Bergh et al. [1]. The ratio is close to that (i.e. 12.76) calculated by Guemes [2] based on data extracted from 53 studies. The high abundance of viruses has been reported in many other environments. Previous work brought the estimated total number of viruses on earth to 1031 and the total mass of 3.95×10^{15} g [2]. However, research on the diversity of viruses remains a bottleneck mainly due to the lack of broad-spectrum marker genes for virus identification [3].

Based on their extraordinary abundance and diversity, viruses are able to significantly affect biogeochemical processes on earth. In the ocean, they are the primary predators of microbial organisms and their lysis results in the release of dissolvable organic compounds from their hosts to surrounding environments. The process is so-called viral shunt [4]. Apart from increasing net primary productivity by feeding heterotrophic microbes via released carbon dioxide and organically complexed iron, viral shunt has a more profound influence on ecosystem because of the release of organic gases (e.g. Dimethyl sulfide, Evans et al., 2007 [5] which impact global climate by a DMS-climate feedback loop [6].

Further, viruses are able to shape the diversity of microbial communities [7]. In nature, viruses sustain microbial species diversity through 'killing the winner' strategy [8]. In this scenario, virus-induced lysis activities on dominant microbial species enable the co-existence of less competitive ones. Further development of this model [9] shows that viral lysis even does not affect microbial abundance. On the other hand, virus-mediated gene transfer is important for the genetic or functional microbial biodiversity and contributes partly to the emergence of new species [7], [10].

2. IN SILICON IDENTIFICATION OF PHAGE-HOST INTERACTIONS

Spacers identified in CRISPR regions of bacterial genomes and tRNA matches are two man culture-independent computational approaches used to link phage and bacteria and many tools

have been developed based on these two methods. CRISPR system is the adaptive immune system against phage infection by bacteria and archaea [11]–[13]. CRISPR regions consist of multiple spacers (25–75 bp long) which thought to be derived from viral genomes [12]. These spacers can be used for recognition of infecting phages by microbes and therefore are putative sequence signature of phage-host interactions [14]. By far, the CRISPRs-based prediction for phage-host relationships has been adopted for the diverse ecosystems. Edwards et al. [14] previously pinpointed that the accuracy of CRISPR matches for identification of phage-host interaction is highly depended on the number of mismatches used. The parameter in the project where linkages predicted by CRISPRs matches were found is 3, and according to Edwards, the quality of this method should be high with only three mismatches being allowed.

Previously, the tRNAs in phage genomes were assumed to be recruited by lysogenic phages for better integration into host genomes [15]. Conversely, Marc Bailly-Bechet et al. (for details see [16]) proposed that phage uses viral tRNAs for adjustment of their usage of codon towards their hosts' instead of better integration. Though there is no evaluation so far for the quality of prediction of phage-host relationship by tRNAs matches, in that project, 94% of linkages identified by tRNAs matches can also be predicted by CRISPRs matches, which indicates that tRNAs matches are capable of giving highly reliable results.

3. AMGS REDIRECTING CELLULAR METABOLISM TO MAXIMISE VIRAL PRODUCTION

During viral predation, phages can pick up functional or metabolic genes from hosts, which are termed as Auxiliary metabolic genes (AMGs) [17], [18]. These repurposed versions of host-genes are evolving separately to improve viral fitness and sometimes returned to microbial genomes. AMGs are supposed to overcome metabolic bottlenecks of the hosts or reprogram the metabolism of host cells [17], [18], [21], [22]. Large-scale metagenomic analysis identified >50 metabolic pathways encoded by viral-enriched (see Enav et al., 2014 for details) AMGs. Most of these pathways are closely connected to purine and pyrimidine metabolism pathways. This implies that reprogramming of host metabolism driven by AMGs might enhance nucleotide biosynthesis which promotes viral replication. Viral *psbA* genes, encoding photosystem II protein D1 [23]–[25] sustain host photosynthesis and manipulate host metabolism to favour progeny phages production [26]. Transcriptional analysis [27] revealed that during the viral infection by cyanophage Syn9 in several *Synechococcus* hosts, within the first hour of infection, the cellular machinery has been repurposed for viral production.

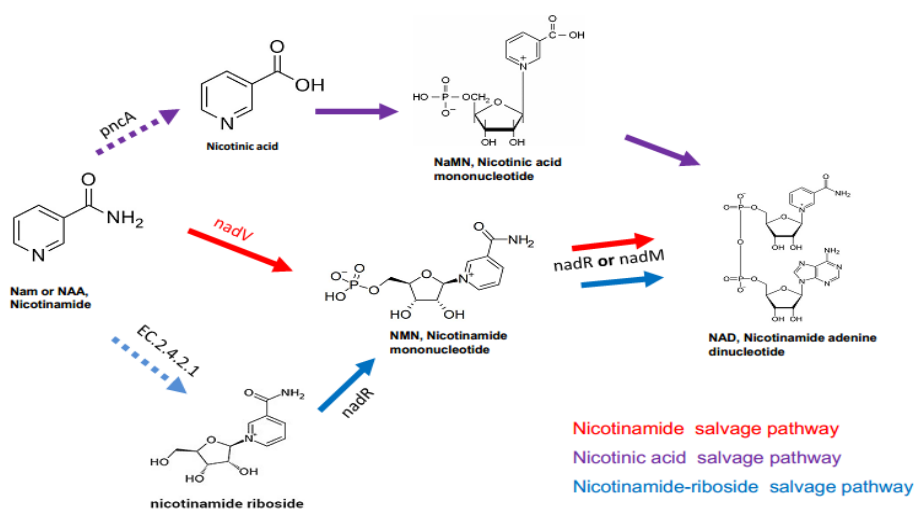


Figure 1. Salvage biosynthesis of NAD, adapted from Gazzaniga, 2009

In an unpublished study, we generated a highly reliable dataset using data extracted from virus-host database and several research projects and utilized the dataset to reveal compensation roles by viral-exclusive AMGs (i.e. viral genes that have functions that the host do not have). Finally, in several phage-host interactions, we identified a few viral-exclusive AMGs that later were annotated as NadV. The early expression of viral nadV encoding genes has been reported [28] during infection in *V. parahaemolyticus* by KVP40 and the those genes were supposed to complement the ability to scavenge nicotinamide for NAD biosynthesis of a mutant bacterial strain.

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