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> ONE MONTH, ONE PROTEIN <

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between you and me

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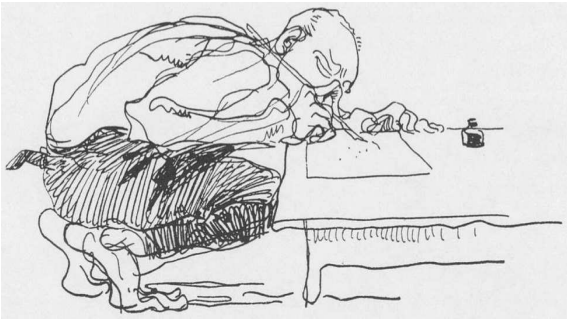
Communication has a purpose and is usually selfish. Humans have raised it to the level of entertainment in the form of books, exhibitions, politics and plays, and to while away time over smoked salmon and a glass of wine. More often than not, however, organisms communicate for survival reasons – flowers let off scent to attract pollinisers, birds whistle to seduce partners, wolves howl to gather for a hunt, ants sting to ward off predators. Reproduction and food are at the heart of communication, and have moulded it into many shapes in Nature. Messages are exchanged using noises, colours, smells and thorns, for instance, but there are other ways of passing on information that are less obvious. Pheromones are an example. Recently, scientists discovered that a certain type of virus is able to tell its progeny when to infect a host or not, depending on the concentration of a protein that has been dubbed arbitrium peptide.



by Heinrich Kley (1863-1945)

Why would a virus choose not to infect? Viruses are usually presented as entities whose sole aim is to invade their hosts and proliferate. Many pathogenic viruses will indeed infect every cell they can if left unhindered. There seem to be a few enlightened viruses, however, that will make sure there are always plenty of hosts left so that - generations later - their progeny can reproduce. They do this by halting infection for a period, during which time the host itself can multiply, thus "unconsciously" providing the virus with future fodder. This is the system that bacteriophage phi3T seems to have adopted to guarantee its survival, and it does it via the arbitrium - Latin for "decision" - peptide.

Bacteriophages - viruses that infect bacteria - are the most common and varied entities on earth, and are found wherever bacteria are present, notably in soil, animal intestines and sea water. The British bacteriologist Ernest Hanbury Hankin (1865-1939) was the first to report, in 1896, that something in the waters of the Ganges and Yamuna rivers in India had antimicrobial action against cholera, which could also explain the rivers' mysterious healing powers. Twenty years later, another British bacteriologist Frederick Twort (1877-1950) discovered a small agent that could infect and kill bacteria. He also observed that the agent needed the bacteria for its growth, but he didn't know if the agent was an enzyme, a stage in the bacterial cycle or a virus. He described his findings in The Lancet but his research was interrupted by World War I, and he never followed up afterwards. In 1917, and independently, the Canadian microbiologist Félix d'Hérelle announced that he had discovered an "invisible, antagonistic microbe of the dysentery bacillus" that he called "bacteriophage", and the name stuck.

Bacterial viruses infect their hosts in two different ways. Once anchored to the cell's membrane, they inject their genome that has one of two distinct fates. Either the viral genome makes immediate use of the host's machinery and produces viral progeny, ultimately causing it to burst (lysis) as they are released. Or the

viral genome is integrated into the bacterial genome and remains silent (lysogeny), as it awaits the right moment to trigger off growth. In so doing, the host becomes immune to infection by the same virus. But when is it the right moment to stop infection? And how is such a decision taken?

Communication among bacteria is typically based on secreted peptides and their receptors that are either membrane-bound or intra-cellular. The same kind of system seems to exist between a virus and its host. When bacteriophage phi3T infects the Bacillus host cell, it secretes a peptide (AimP) that is matured into a six amino-acid long peptide - the arbitrium peptide. The more phi3T multiplies in cells, the more arbitrium peptide is secreted into the medium. As long as arbitrium concentration is low, the progeny phages will continue to multiply and lyse their host cells; when arbitrium peptide concentration becomes high however, the phages will stop multiplying for a while and lysogenize their host cells.

How do progeny phages measure arbitrium concentration? Thanks to an intracellular arbitrium communication peptide receptor: AimR. When phage phi3T infects Bacillus, both AimP and AimR are expressed. AimP is secreted, while AimR binds as an active dimer to a single site on the phage genome to promote cell lysis. At one point, the extracellular concentration of arbitirium peptide is such that the peptide is internalized via a transporter into Bacillus and binds to AimR. Binding alters the oligomeric state of AimR, which loses grasp of the DNA and becomes an inactive monomer. Arbitrium peptide thus acts as a sort of on/off lysis/no lysis switch by modifying the structure of AimR.

The arbitrium lysis/no lysis switch is a profoundly self-centred but very elegant way for a phage to estimate the amount of recent infections and whether the consequences of further infection will be fruitful for its species or not. This kind of communication does not seem to be particular to phi3T but is probably shared by a large group of Bacillus phages. Other phages could rely on other peptides, however, in which case each phage may literally have its own language. Moreover, the system is probably not limited to bacteriophages but could be used by viruses whose hosts are eukaryotes.

How the lysis/no lysis switch works in detail will help scientists understand how infections appear, at which rhythm, and how certain phages could be used as an alternative to antibiotics for instance. Phages have been used in this way for almost a century in Central Europe for example, and they were used in the USA during the 1920s and 30s for treating bacterial infections on burns or wounds - but the human body develops antibodies against phages very quickly which is why they are not more widely used. Currently phages are used on food products - poultry, meat and cheese - to kill off bacteria, in horticulture to protect plants, and as preventive medicines for medical devices in clinics. Researchers are also looking for ways to engineer bacteriophages that could beat antibiotic resistance, and counteract bioweapons and toxins, such as anthrax and botulism. The ways Nature has of creating dialogue between organisms are rich and imaginative, and, will no doubt continue to be an essential source of inspiration to scientists.

Cross-references to UniProt

Arbitrium peptide, *Bacillus phage phi3T* (Bacteriophage phi-3T) : P0DOE2
Arbitrium communication peptide receptor, *Bacillus phage phi3T* (Bacteriophage phi-3T) : P0DOE3

References

1. Erez Z., Steinberger-Levy I., Shamir M., Doron S., Stokar-Avihail A., Peleg Y., Melamed S., Leavitt A., Savidor A., Albeck S., Amitai G., Sorek R.
Communication between viruses guides lysis-lysogeny decisions
Nature 541:488-493(2017)
PMID: 28099413