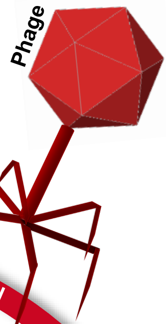
Gut Phageomics

Science Foundation Ireland — sfi — For what's next

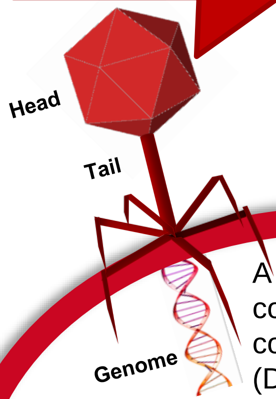
apc Microbiome Institute — Interfacing Food & Medicine

1 **A lytic phage recognises a target bacterial cell**



A **bacteriophage** (phage) is a virus that infects bacteria and multiplies within the cell, eventually leading to its death and the release of up to 200 new phage particles. Phages are the most abundant and diverse entities on Earth. There are more than 100,000,000,000,000 (10^{14}) in the human body, most of which are in the gut. Phage come in many shapes and sizes, but all are tiny (20-200 nm) – smaller than the width of a hair.

2 **The phage binds to bacterial surface and injects its genome**



A typical phage consists of a head containing its genome (DNA or RNA) and a tail, which attaches to the target bacterial cell. The phage injects its genome and hijacks the bacterial metabolism to make new copies of itself. Phages multiply and cause bacterial cell death (**lytic** replication) or insert into the bacterial genome and multiply along with the host cell (**lysogenic** replication).

Very powerful microscopes (electron microscopes) can be used to visualise phages. Here we see many attached to a bacterial cell.

3 **During lytic replication, phage genomes and proteins are synthesised and are assembled into new phages. Eventually the bacterial cell bursts, releasing new lytic phages.**

Phage therapy is the use of lytic phages to kill harmful bacteria. Most phages only target a single bacterial species and so cause less damage to other bacteria. For this reason, they are viable alternatives to antibiotics, as they can kill the target bacterium without damaging potentially beneficial bacteria in the human host.

100 Years of phage research – the story so far

Bacteriophages were independently discovered by Frederick Twort in 1915 and Félix d'Hérelle in 1917. d'Hérelle pioneered the concept of 'phage therapy' as a treatment for diseases such as typhoid, dysentery and cholera, and infections such as septicaemia. Phage therapy is still practiced in Georgia, Poland and Russia. However, when broad spectrum antibiotics were discovered in 1941 and marketed widely, western scientists used phage primarily as research tools. More than 10 Nobel prizes have been awarded for phage research! There has been a resurgence in interest in phage therapy, as many bacteria have developed resistance to antibiotics. Also our understanding of the important role of the human microbial community (microbiota) in health has led to a search for 'narrow spectrum' antimicrobials, which can treat infections without causing 'collateral' damage to the microbiota. Phage may provide an ideal solution.

Medicinal phage therapy vials from Georgia.

Research at the APC Microbiome Institute Gut Phageomics Lab

The Gut Phageomics laboratory seeks to exploit phage in several ways to benefit human health:

- **Phage therapy**

We have isolated a number of phages from human volunteers. These phages could be used to treat infections caused by pathogenic bacteria such as *Pseudomonas aeruginosa* (associated with cystic fibrosis), *Streptococcus mutans* (leading cause of tooth decay) and *E.coli* (known to cause serious food poisoning), amongst many others.

Phages kill bacteria in a petri dish

- **Phage as diagnostics**

Since phages are the most abundant members of the human microbiota, we can also use them to assess the diversity and stability of these complex communities. We may even be able to use them to diagnose certain disease states.

- **Phage to restore diversity**

Predators are important to maintain diversity in any ecosystem. Certain disease states are associated with a low diversity microbiota. Introducing phage into these low diversity environments could potentially increase diversity and restore health.