NEWSLETTER

Bacteriophages as Treatments for Bacteria-based Infectious Diseases

MIRCORE NEWS & EVENTS

- **Middle school biology workshop:** November 15th
- Talk from **Dr. Adam Lauring,** section head of infectious disease at the University of Michigan.
- In person meetings at University of Michigan, Scripps, and NorCal area
- **New volunteer login site!**

2025 MICROGRANT RECIPIENT: DR. RISHI CHANDERRAJ

Every year, miRcore selects a scientific cause for which microgrants- funding, are allocated. For 2025 and 2026, miRcore, with the theme of **infectious disease research,** has selected **Dr. Rishi Chanderraj's** research on the microbiome and antibiotics as the recipient.
Antibiotics, a staple treatment for curing infectious diseases primarily related to **bacteria**, can also have the adverse effect of ravaging your **microbiome**, which is critical to the proper functionality and **health of the gut**. Some of these effects can cause inflammation, organ failure, and even **death**. Dr. Chanderraj's research aims to investigate various antibiotics and their effects on the human microbiome, possibly leading to a **newfound understanding** of how to make antibiotic treatments more effective while maintaining the precarious but critical balance inherent in our gut microbiome.

INTRODUCTION

Antibiotic-resistant bacteria are on the rise, and **many bacteria no longer respond to the medicines we rely on.** This pressing issue opens the door for a surprising alternative: **bacteriophages - viruses that only attack bacteria.** Here's how bacteriophages work and why scientists think they could be part of the future of medicine.

BACKGROUND

- **Bacteriophages** are **viruses** that only infect and multiply in **bacterial cells**
- They are both populous in the environment and diverse in their characteristics
- **Antibiotic-resistant bacteria** are on the rise and make it difficult for **infectious diseases** to be treated
- Opens the door for **phage therapy** as an alternative solution to treating **bacterial infections**

SYMPTOMS & MECHANISMS

- **Symptoms** vary based on the type of **bacterial infection**
- Phages do not affect humans unless humans obtain **phage-infected bacteria**
- Phages can use either **lytic** or **lysogenic cycles** that hijack the bacteria's processes, which eventually lead to the death of the bacteria

THE PATHOGEN

A **pathogen** is any biological agent that can infect another **organism**.

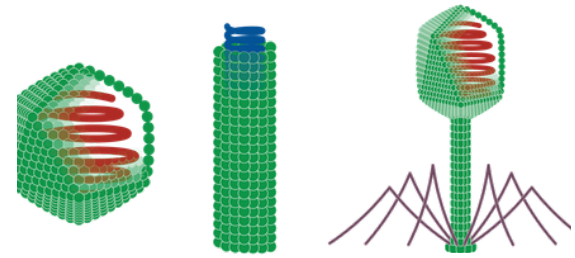
In this case, the pathogen is the bacteriophage, because it infects bacteria. Specifically, it's a **nucleic acid genome contained in a shell of phage-encoded capsid proteins.** Regarding hosts, it is species specific.

The bacteriophage has three main formations:

- **Icosahedral head** with a tail (20-sided!)
- **Icosahedral head** without a tail
- **Filamentous** form

Transmission

The pathogen infects by attaching to the bacteria and injecting genetic material.



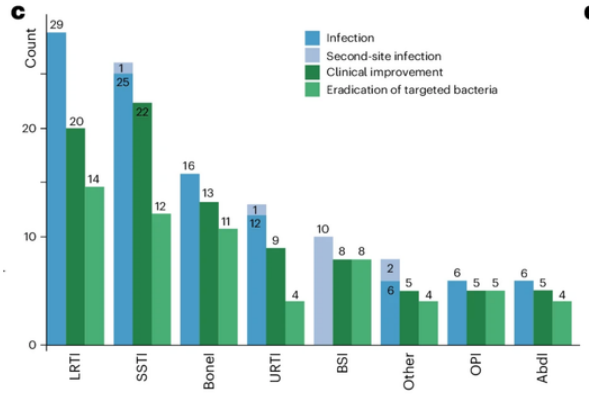
Icosahedral Filamentous Head-tail

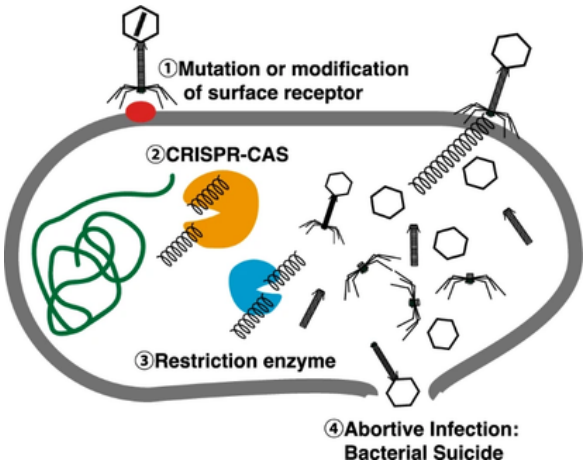
LIFE CYCLES: LYSIC VS LYSOGENIC

- **Lysic**: Phage uses the host bacteria's **ribosomes** to manufacture proteins that can be converted to **viral genomes** and **capsid proteins**, assembling into replications of the parent phage. After the **host cell** dies the bacteriophage are released to infect other cells
- **Lysogenic**: The genome of the phage is mixed with the **bacterial cell chromosome** or not but either way is replicated and **inherited** by **daughter bacterial cells** without the cells dying off. Phages going through the lysogenic cycle can switch to the the lytic cycle and kill their host, particularly when environmental conditions are fluctuating
- **Bacteria-infected** individuals most affected as phages contributing to their condition have impact on how severe symptoms are

RECENT BREAKTHROUGHS

- The past few years have seen a **resurgence in bacteriophage research,** with many notable papers and articles released in the 2020s
- Research into bacteriophages is new overall because it has been realized **how resistant bacteria can be to antibiotics**
- In a large-scale study, 252 bacterial isolates from the human gut were determined and prepared
- Most gut bacteriophages were **dormant**, but gut cells can increase their activation rate in order to trigger them and **reveal their functions**
- A Belgian study analyzed 100 cases of individualized phage therapy
- 77% of cases showed **clinical improvement**, while 61% of cases showed **bacterial eradication**
- **Antibiotics** were also revealed to have **high compatibility** when used with phage therapy



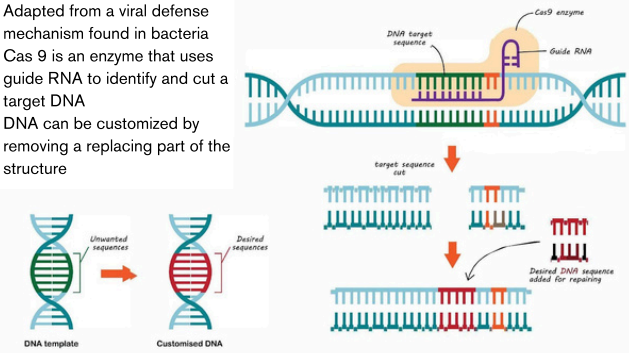


THERAPIES AND VACCINES

- Phage-displayed vaccines work by expressing antigens directly on the surface of bacteriophages. This strategy leverages several natural advantages of phage particles - including **strong immune enhancing capabilities, low-cost and scalable production, and exceptional stability -** making them a promising platform for next-generation vaccines.
- While bacteriophage-based therapies require regular monitoring to ensure continued effectiveness, they also provide remarkable benefits: **phages can counteract or even reverse bacterial resistance to antibiotics.**
- By selectively targeting resistant bacteria or restoring their susceptibility to existing drugs, phage therapy provides a **powerful tool against some of the most challenging infectious diseases.**

How does CRISPR-Cas 9 work?

- Adapted from a viral defense mechanism found in bacteria
- Cas 9 is an enzyme that uses guide RNA to identify and cut a target DNA
- DNA can be customized by removing a replacing part of the structure



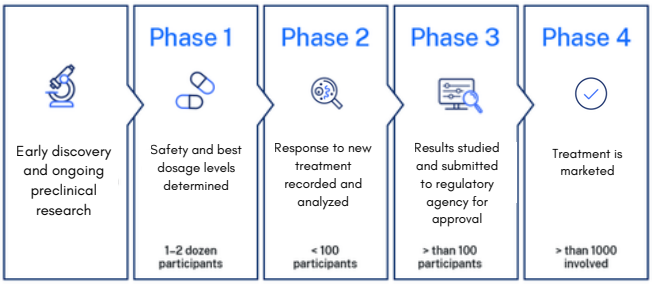
TECHNOLOGY SPOTLIGHT

- **AI generated viral genomes** that were used to synthesize bacteriophages, and may hasten the process of identifying phages that can guarantee optimal effects against a specific bacteria
- **CRISPR-Cas9** is one basis of gene technology with bacteriophages; for example, LOCUS makes **precision medicine and therapeutics** based on that method
- Case: **Diabetic foot osteomyelitis (DFO)** is an infectious **complication of bone and tissue** in the foot caused by **diabetes**, whose trauma, ulcers, and poor blood circulation can cause amputation if not treated. As a result, APT released the DANCE trial to combat **specific infectious bacteria related to DFO**.

FUN FACTS

Scientists are careful with **dosing** phage **vaccines** as bacteriophages multiply within the body. There must be sufficient support to remove the "guts" of bacteria once bacteriophages kill the targeted bacteria.
- To understand the scope of bacteriophage treatment, one must know the phases of **clinical administration.**

- Phase 1 trials determine how **safe** a **drug** is. They take several months.
- Phase 2 trials determine the **effectiveness** and **side effects** of a drug. They can last up to 2 years.
- Sometimes, Phase 1/2 trials are conducted, which gather safety and effectiveness from a small group at the **same time** to **speed up** the process.
- Phase 3 trials continue **additional observations** of a drug in addition to **comparing** it to related treatments and confirming its **efficacy**. They can last up to 4 years.





FELIX D'HERELLE

PEOPLE AND CAREERS

- Félix d'Herelle found that bacteriophages were associated with **diarrheal illnesses** and also the **recovery** from such illnesses
- Proposed using phages as treatment for bacterial infections
- Frederick Twort observed "**glassy transformation of bacteria**."



FREDERICK TWORT

CALL TO ACTION

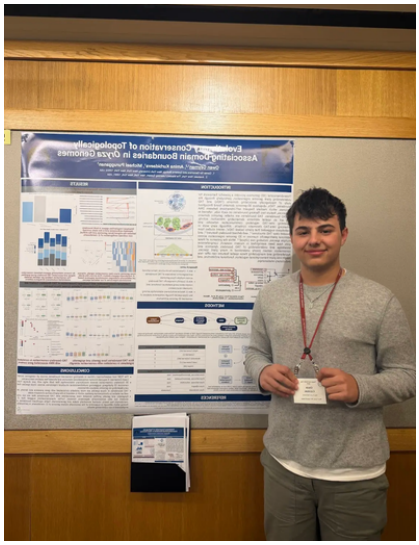
- With the **promising output** of bacteriophage research, more people can volunteer for clinical trials, raise public awareness, and allow some form of federal investment.
- Fundamentally, a **solid foundation** for which research can proceed is necessary.
- **Anyone can make an impact!** You can advocate for **funding and support** for the efforts of people who research, and with the help of others, form a **collaborative community for the cause**.



STUDENT PROJECT HIGHLIGHT

Owen Geyman, a fellow miRcorer, has been working on a fairly interesting research project with an interesting focus. **Inspired by the power and capabilities of 3D genome analysis, he takes a unique approach by investigating the way the DNA is folded.**





More specifically, **he analyzes the edges of rice species' TAD boundaries,** which can be described as **buffer zones** to prevent interactions between DNA "neighborhoods", but also characteristically mark where a **folded DNA "neighborhood"** ends and begins.

Owen utilizes advanced techniques such as Hi-C and 3D genome organization to see what parts of the DNA touch and how DNA folds within the nucleus. **This allows him to see which of these TAD boundaries change, disappear, or rearrange over evolution**, and can thus attempt to determine how **folding patterns kept across species of rice may play a crucial role in function or regulation.**



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