THE COLLEGE OF WOOSTER

Host Species Range Expansion as a Risk Factor of Polyvalent Phage Applications in Emerging Phage Therapeutic Techniques

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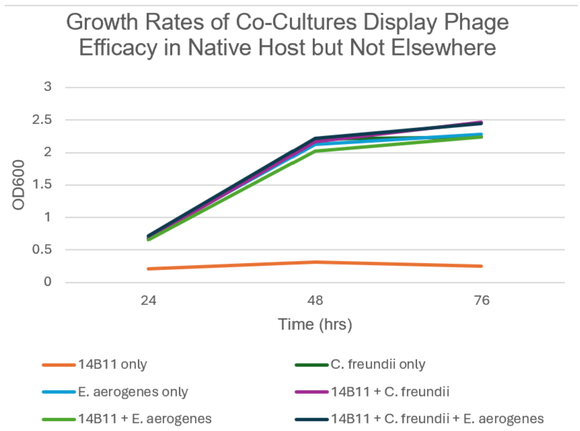
Introduction – Why Polyvalent Phages?

- Bacteriophages were first discovered and envisioned for antibiotic applications by Felix d'Herelle in the early 20th century. However, they fell out of favor when broad-spectrum antibiotics such as penicillin were popularized.[1]
- However, with the emergence of multi-drug-resistant bacterial threats that broad-spectrum antibiotics are ineffective against,[2] there has been a resurgence of interest in phage therapy.[3]
- For the purposes of this study, monovalent phages are defined as phages which infect a single species of bacteria, while polyvalent phages can infect multiple species or even genera.[4]
- A key property common to polyvalent phages is an abundance of hypervariable SNP sites in the genes coding for the tail fiber and tail tubular regions, two regions heavily involved in the phage binding to receptors on the surface of bacteria to infect them.[5]
- While increased adaptability to resistance-mutations in bacterial receptor structures may seem beneficial, this property, which allows polyvalent phages to expand their "host-range", or the number of species/genera they can infect, could make therapeutic applications more risk-prone, as many microbiotal bacteria serve a beneficial, symbiotic purpose, and I hypothesize that with the wrong mutation or combination of mutations in the phage, these "good bacteria" may be prone to cross-infection.

Methodology – Developing the Co-Culturing Protocol



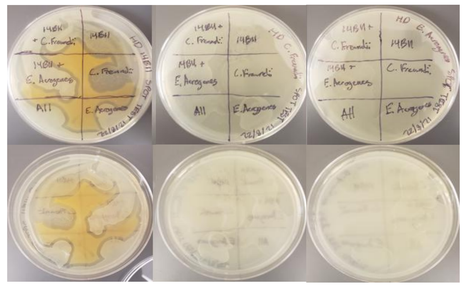
- In the above procedure, a monovalent phage control, PC1, was added to various tubes seeded with overnight cultures and these were allowed to develop for three days.

- This protocol was refined for the polyvalent phage phi6, with variable starting volumes of overnight culture compared to LB and daily re-seeding of cultures along with inoculation with phage samples from previous tubes.

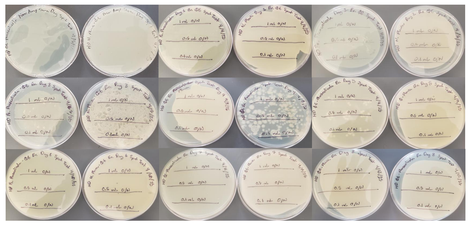
Brief Acknowledgement

- To the Dennehy lab, for providing phi6 and host strain.

Results – No Expansion in Short-Term



- The monovalent phage showed no clearance except on original control, though bacterial regrowth occurred.



- The polyvalent phage showed similar results, though contamination of the viral samples had to be overcome.

Conclusion – Needs Further Investigation

- Not enough short-term data, should have three weeks worth at least.
- Long-term investigation important for verifying safe treatment of chronic infections.

References

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